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(54) Title: COPPER-CATALYZED FORMATION OF CARBON-HETEROATOM AND CARBON-CARBON BONDS

(57) Abstract: The present invention relates to copper-catalyzed carbon-heteroatom and carbon-carbon bond-forming methods. In certain embodiments, the present invention relates to copper-catalyzed methods of forming a carbon-nitrogen bond between the nitrogen atom of an amide or amine moiety and the activated carbon of an aryl, heteroaryl, or vinyl halide or sulfonate. In additional embodiments, the present invention relates to copper-catalyzed methods of forming a carbon-nitrogen bond between a nitrogen atom of an acyl hydrazine and the activated carbon of an aryl, heteroaryl, or vinyl halide or sulfonate. In other embodiments, the present invention relates to copper-catalyzed methods of forming a carbon-nitrogen bond between the nitrogen atom of a nitrogen-containing heteroaromatic, e.g., indole, pyrazole, and indazole, and the activated carbon of an aryl, heteroaryl, or vinyl halide or sulfonate. In certain embodiments, the present invention relates to copper-catalyzed methods of forming a carbon-oxygen bond between the oxygen atom of an alcohol and the activated carbon of an aryl, heteroaryl, or vinyl halide or sulfonate. The present invention also relates to copper-catalyzed methods of forming a carbon-carbon bond between a reactant comprising a nucleophilic carbon atom, e.g., an enolate or malonate anion, and the activated carbon of an aryl, heteroaryl, or vinyl halide or sulfonate. Importantly, all the methods of the present invention are relatively inexpensive to practice due to the low cost of the copper comprised by the catalysts.

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COPPER-CATALYZED FORMATION OF CARBON-HETEROATOM AND CARBON-CARBON BONDS

Background of the Invention

- 5 N-Aryl amines and amides are important substructures in natural products and
industrial chemicals, such as pharmaceuticals, dyes, and agricultural products. Palladium-
catalyzed methods for the N-arylation of amines and amides are now widely-exploited for
the synthesis of arylamine and N-aryl amide moieties in pharmaceuticals, materials with
important electronic properties, and ligands for early metal catalysts. Likewise, the
10 palladium-catalyzed coupling to form carbon-carbon bonds between an aryl or vinyl halide
and a carbon nucleophile is widely used. See, e.g., Stille, J. K. Angew. Chem., Int. Ed.
Engl., 25:508-524 (1986); Miyaura, N. et al., Chem. Rev., 95:2457-2483 (1995); Negishi,
E. Acc. Chem. Res., 15:340-348 (1982).

However, the ever-increasing cost of palladium detracts from the allure of these powerful methods. Consequently, a need exists for a general and efficient catalytic method for synthesizing N-aryl amines and amides, from aryl halides and the corresponding amines and amides, based on a catalyst that does not comprise a rare, costly transition metal, such as palladium. Likewise, a need also exists for a general and efficient catalytic method for forming carbon-carbon bonds between an aryl or vinyl halide and a carbon nucleophile, based on a catalyst that does not comprise a rare, costly transition metal, such as palladium.

In 1998, bulk palladium sold on the international metal market for roughly five-thousand-times the cost of bulk copper. Therefore, based on catalyst cost, the aforementioned transformations would be orders of magnitude more appealing if they could be achieved with catalysts comprising copper in place of palladium.

25 *Summary of the Invention*

The present invention relates to copper-catalyzed carbon-heteroatom and carbon-carbon bond-forming methods. In certain embodiments, the present invention relates to copper-catalyzed methods of forming a carbon-nitrogen bond between the nitrogen atom of an amide or amine moiety and the activated carbon of an aryl, heteroaryl, or vinyl halide or sulfonate. In additional embodiments, the present invention relates to copper-catalyzed methods of forming a carbon-nitrogen bond between a nitrogen atom of an acyl hydrazine and the activated carbon of an aryl, heteroaryl, or vinyl halide or sulfonate. In other embodiments, the present invention relates to copper-catalyzed methods of forming a

carbon-nitrogen bond between the nitrogen atom of a nitrogen-containing heteroaromatic, e.g., indole, pyrazole, and indazole, and the activated carbon of an aryl, heteroaryl, or vinyl halide or sulfonate. In certain embodiments, the present invention relates to copper-catalyzed methods of forming a carbon-oxygen bond between the oxygen atom of an alcohol and the activated carbon of an aryl, heteroaryl, or vinyl halide or sulfonate. The present invention also relates to copper-catalyzed methods of forming a carbon-carbon bond between a reactant comprising a nucleophilic carbon atom, e.g., an enolate or malonate anion, and the activated carbon of an aryl, heteroaryl, or vinyl halide or sulfonate. Importantly, all the methods of the present invention are relatively inexpensive to practice due to the low cost of the copper comprised by the catalysts.

Brief Description of the Figures

Figure 1 tabulates the results of various copper-catalyzed arylations of benzylamine using aryl iodides, and the reaction conditions employed.

Figure 2 tabulates the results of copper-catalyzed arylations of various amines using iodobenzene, and the reaction conditions employed.

Figure 3 tabulates copper-catalyzed arylations of various amines using various aryl iodides, and the reaction conditions employed.

Figure 4 tabulates copper-catalyzed aminations of bromobenzene using *n*-hexyl amine and various substituted phenols as ligands.

Figure 5 tabulates copper-catalyzed aminations of 1-bromo-3,5-dimethylbenzene using *n*-hexyl amine and various copper complexes.

Figure 6 tabulates copper-catalyzed aminations of 1-bromo-3,5-dimethylbenzene using *n*-hexyl amine in various solvents.

Figure 7 tabulates copper-catalyzed aminations of bromobenzene using *n*-hexyl amine and various ligands.

Figure 8 tabulates copper-catalyzed aminations of 1-bromo-3,5-dimethylbenzene using *n*-hexyl amine and various ligands without solvent.

Figure 9 tabulates copper-catalyzed aminations of 1-bromo-3,5-dimethylbenzene using *n*-hexyl amine with low catalyst loading.

Figure 10 tabulates copper-catalyzed aminations of various functionalized aryl bromides.

Figure 11 tabulates copper-catalyzed aminations of various *ortho*-substituted, dibromo-substituted and heterocyclic aryl bromides.

Figure 12 tabulates copper-catalyzed aminations of various functionalized aryl bromides using various amines without solvent.

5 **Figure 13** tabulates copper-catalyzed arylations of indole in dioxane using 4-bromotoluene and various ligands.

Figure 14 tabulates copper-catalyzed arylations of indole in toluene using 4-bromotoluene and various ligands.

10 **Figure 15** tabulates copper-catalyzed arylations of indole in toluene using 2-bromotoluene and various ligands.

Figure 16 tabulates copper-catalyzed arylations of indole in toluene using 2-bromotoluene and various ligands.

Figure 17 tabulates copper-catalyzed arylations of N-phenyl acetamide in dioxane using 3,5-dimethylphenyl iodide and various ligands.

15 **Figure 18** tabulates copper-catalyzed arylations of 2-pyrrolidinone in toluene using 3,5-dimethylphenyl iodide and various ligands.

Figure 19 tabulates copper-catalyzed arylations of N-benzyl formamide in toluene using 3,5-dimethylphenyl bromide and various ligands.

20 **Figure 20** tabulates copper-catalyzed arylations of N-methyl formamide in toluene using 3,5-dimethylphenyl iodide and various ligands.

Figure 21 tabulates copper-catalyzed arylations of N-methyl formamide in toluene using 3,5-dimethylphenyl iodide and various sources of copper.

Figure 22 tabulates copper-catalyzed arylations of N-methyl para-toluenesulfonamide in toluene using iodobenzene and various bases.

25 **Figure 23** tabulates copper-catalyzed arylations of n-hexyl amine in DMF using diethyl salicylamide as the ligand and various bases.

* **Figure 24** tabulates copper-catalyzed arylations of benzyl amine in isopropanol using ethylene glycol as the ligand and various bases.

30 **Figure 25** tabulates copper-catalyzed arylations of benzyl amine in isopropanol using various diols as the ligand.

Figure 26 tabulates copper-catalyzed arylations of n-hexyl amine in n-butanol using various ligands.

Detailed Description of the Invention

The present invention relates to copper-catalyzed carbon-heteroatom and carbon-carbon bond-forming methods. In certain embodiments, the present invention relates to copper-catalyzed methods of forming a carbon-nitrogen bond between the nitrogen atom of an amide or amine moiety and the activated carbon of an aryl, heteroaryl, or vinyl halide or sulfonate. In additional embodiments, the present invention relates to copper-catalyzed methods of forming a carbon-nitrogen bond between a nitrogen atom of an acyl hydrazine and the activated carbon of an aryl, heteroaryl, or vinyl halide or sulfonate. In other embodiments, the present invention relates to copper-catalyzed methods of forming a carbon-nitrogen bond between the nitrogen atom of a nitrogen-containing heteroaromatic, e.g., indole, pyrazole, and indazole, and the activated carbon of an aryl, heteroaryl, or vinyl halide or sulfonate. In certain embodiments, the present invention relates to copper-catalyzed methods of forming a carbon-oxygen bond between the oxygen atom of an alcohol and the activated carbon of an aryl, heteroaryl, or vinyl halide or sulfonate. The present invention also relates to copper-catalyzed methods of forming a carbon-carbon bond between a reactant comprising a nucleophilic carbon atom, e.g., an enolate or malonate anion, and the activated carbon of an aryl, heteroaryl, or vinyl halide or sulfonate. Importantly, all the methods of the present invention are relatively inexpensive to practice due to the low cost of the copper comprised by the catalysts.

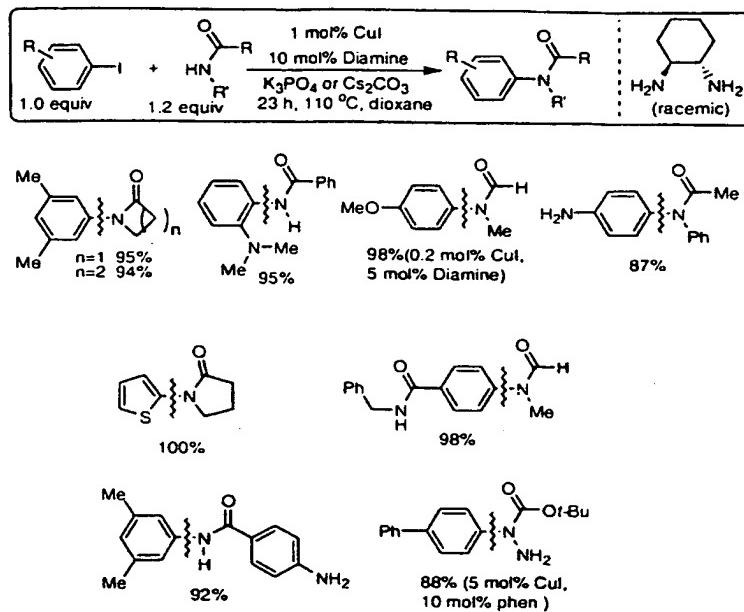
20 Cu-Catalyzed N-Arylation of Amides

The coupling of aryl iodides and bromides with amides, the so-called Goldberg reaction, is not very general in terms of substrate scope, often requiring stoichiometric quantities of copper complexes. Moreover, as with the related Ullmann reaction, the reaction conditions for the Goldberg reaction are often quite harsh, with required temperatures as high as 210 °C. Nevertheless, the methods of the present invention effect these reactions using only 1 mol% CuI and have successfully used as little as 0.2 mol% CuI.

*In many instances, a system derived from 1% CuI, 10% (racemic)-*trans*-cyclohexane-1,2-diamine, and K₃PO₄ or Cs₂CO₃ provides an outstanding catalyst for the amidation of aryl iodides. Importantly, CuI is an air-stable Cu(I) source. As can been seen in the

30 Exemplification, the process enjoys broad substrate scope with respect to the aryl iodide component. Notably, the arylation of a 2° amide-containing substrate and of 4-iodoaniline are possible; Pd-catalyzed C-N bond-forming processes with substrates that contain these

functional groups are not successful. We have also been able to N-arylate N-BOC hydrazine. Further, this process provides a convenient entry into the synthesis of hydrazines, and, therefore, a means to access Fischer indole substrates and other heterocycle synthons.



5

The copper-catalyzed methods of the present invention allow the amidation of aryl bromides. These reactions typically use 1-20 mol% CuI; for example, in one embodiment, 1 mol% CuI was used, yielding the product in 90% yield. Additionally, the coupling of an unactivated aryl chloride with an amide has also been achieved using the methods of the present invention.

The methods of the present invention also work well for the coupling of aryl iodides with primary amides; in fact, there appear to be no limitations on the nature of the acyl substituent (R in RC(O)NH_2). With respect to 2° amides, N-acyl anilines and lactams are preferred substrates. N-formyl amides derived from alkyl amines are satisfactory substrates. Consequently, we believe that steric hindrance influences the outcome of the methods. In embodiments wherein ligand arylation competes with substrate arylation, the use of a 1,10-phenanthroline or an N,N'-dimethyl-1,2-diamine gives improved results.

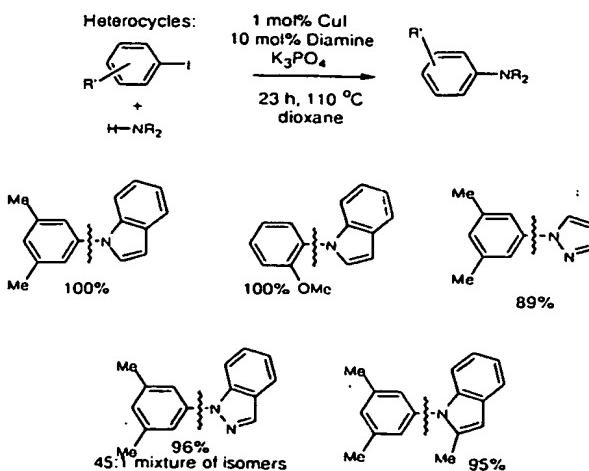
In preferred embodiments, the pK_a of the amide is in the particular range of 20-25, as measured in DMSO. Generally, strong bases are less effective than weak bases in the methods of the present invention; for example, Cs_2CO_3 and K_3PO_4 are efficient bases in

many embodiments. For the coupling of aryl bromides at low catalyst loadings, and for the coupling of aryl chlorides, the use of K_2CO_3 is preferred. These results are consistent with the notion that it is important to keep the concentration of the deprotonated amide low in order to prevent deactivation of the catalyst. Interestingly, to a certain extent, decreasing 5 the catalyst loading does not appear to compromise the reaction efficiency.

Cu-Catalyzed N-Arylation of Heterocycles

In terms of the desirability of the products, some of the most important substrates for the catalyzed N-arylation are nitrogen-containing heterocycles, e.g., pyrrole, and indole. Previous reports of copper-mediated heterocycle N-arylations suffer from limitations similar 10 to those of the Ullmann reaction. Likewise, the Cu-promoted or catalyzed coupling of heterocycles with aryl boronic acids is of limited scope. Moreover, boronic acids are much less attractive as precursors than aryl halides. Accordingly, a general solution to the arylation of heterocycles has been sought for years.

The methods of the present invention allow N-arylation of nitrogen-containing 15 heteroaromatics using 2-haloanisole or 2-methyl indole as one of the coupling partners; in these embodiments, the methods of the present invention afford the desired products nearly quantitatively, whereas the same transformations are very difficult using Pd catalysts. Further, the methods of the present invention enable N-arylation of pyrazole and indazole. Accordingly, the methods of the present invention enable the arylation of a variety of 20 nitrogen heterocycles.



Mild, inexpensive bases, such as K_3PO_4 and K_2CO_3 , are effective in these transformations. These reactions are usually very clean, and arene reduction is typically less

problematic than in corresponding Pd systems. The methods of the present invention are often able to effect the desired coupling with as little as 1 mol% CuI; however, elevated temperatures, e.g., 110 °C, are normally required for the reaction. Nevertheless, in certain embodiments, a method of the present invention provides an N-aryl heteroaromatic in good yield when performed at room temperature.

Definitions

For convenience, certain terms employed in the specification, examples, and appended claims are collected here.

The term "nucleophile" is recognized in the art, and as used herein means a chemical moiety having a reactive pair of electrons. Examples of nucleophiles include uncharged compounds such as water, amines, mercaptans and alcohols, and charged moieties such as alkoxides, thiolates, carbanions, and a variety of organic and inorganic anions. Illustrative anionic nucleophiles include simple anions such as hydroxide, azide, cyanide, thiocyanate, acetate, formate or chloroformate, and bisulfite. Organometallic reagents such as 10 organocuprates, organozincs, organolithiums, Grignard reagents, enolates, acetylides, and the like may, under appropriate reaction conditions, be suitable nucleophiles. Hydride may 15 also be a suitable nucleophile when reduction of the substrate is desired.

The term "electrophile" is art-recognized and refers to chemical moieties which can accept a pair of electrons from a nucleophile as defined above. Electrophiles useful in the 20 method of the present invention include cyclic compounds such as epoxides, aziridines, episulfides, cyclic sulfates, carbonates, lactones, lactams and the like. Non-cyclic electrophiles include sulfates, sulfonates (e.g. tosylates), chlorides, bromides, iodides, and the like

The terms "electrophilic atom", "electrophilic center" and "reactive center" as used 25 herein refer to the atom of the substrate which is attacked by, and forms a new bond to, the nucleophile. In most (but not all) cases, this will also be the atom from which the leaving group departs.

The term "electron-withdrawing group" is recognized in the art and as used herein means a functionality which draws electrons to itself more than a hydrogen atom would at 30 the same position. Exemplary electron-withdrawing groups include nitro, ketone, aldehyde, sulfonyl, trifluoromethyl, -CN, chloride, and the like. The term "electron-donating group", as used herein, means a functionality which draws electrons to itself less than a hydrogen

atom would at the same position. Exemplary electron-donating groups include amino, methoxy, and the like.

The terms "Lewis base" and "Lewis basic" are recognized in the art, and refer to a chemical moiety capable of donating a pair of electrons under certain reaction conditions.

- 5 Examples of Lewis basic moieties include uncharged compounds such as alcohols, thiols, olefins, and amines, and charged moieties such as alkoxides, thiolates, carbanions, and a variety of other organic anions.

The term "Bronsted base" is art-recognized and refers to an uncharged or charged atom or molecule, e.g., an oxide, amine, alkoxide, or carbonate, that is a proton acceptor.

- 10 The terms "Lewis acid" and "Lewis acidic" are art-recognized and refer to chemical moieties which can accept a pair of electrons from a Lewis base.

The term "meso compound" is recognized in the art and means a chemical compound which has at least two chiral centers but is achiral due to an internal plane, or point, of symmetry.

- 15 The term "chiral" refers to molecules which have the property of non-superimposability on their mirror image partner, while the term "achiral" refers to molecules which are superimposable on their mirror image partner. A "prochiral molecule" is an achiral molecule which has the potential to be converted to a chiral molecule in a particular process.

- 20 The term "stereoisomers" refers to compounds which have identical chemical constitution, but differ with regard to the arrangement of their atoms or groups in space. In particular, the term "enantiomers" refers to two stereoisomers of a compound which are non-superimposable mirror images of one another. The term "diastereomers", on the other hand, refers to the relationship between a pair of stereoisomers that comprise two or more 25 asymmetric centers and are not mirror images of one another.

- Furthermore, a "stereoselective process" is one which produces a particular stereoisomer of a reaction product in preference to other possible stereoisomers of that product. An "enantioselective process" is one which favors production of one of the two possible enantiomers of a reaction product. The subject method is said to produce a 30 "stereoselectively-enriched" product (e.g., enantioselectively-enriched or diastereoselectively-enriched) when the yield of a particular stereoisomer of the product is greater by a statistically significant amount relative to the yield of that stereoisomer

resulting from the same reaction run in the absence of a chiral catalyst. For example, an enantioselective reaction catalyzed by one of the subject chiral catalysts will yield an e.e. for a particular enantiomer that is larger than the e.e. of the reaction lacking the chiral catalyst.

The term "regioisomers" refers to compounds which have the same molecular
5 formula but differ in the connectivity of the atoms. Accordingly, a "regioselective process" is one which favors the production of a particular regioisomer over others, e.g., the reaction produces a statistically significant preponderance of a certain regioisomer.

The term "reaction product" means a compound which results from the reaction of a nucleophile and a substrate. In general, the term "reaction product" will be used herein to
10 refer to a stable, isolable compound, and not to unstable intermediates or transition states.

The term "substrate" is intended to mean a chemical compound which can react with a nucleophile, or with a ring-expansion reagent, according to the present invention, to yield at least one product having a stereogenic center.

The term "catalytic amount" is recognized in the art and means a stoichiometric
15 amount relative to a reactant.

As discussed more fully below, the reactions contemplated in the present invention include reactions which are enantioselective, diastereoselective, and/or regioselective. An enantioselective reaction is a reaction which converts an achiral reactant to a chiral product enriched in one enantiomer. Enantioselectivity is generally quantified as "enantiomeric excess" (ee) defined as follows:

% Enantiomeric Excess A (ee) = (% Enantiomer A) - (% Enantiomer B)
where A and B are the enantiomers formed. Additional terms that are used in conjunction with enantioselectivity include "optical purity" or "optical activity". An enantioselective reaction yields a product with an e.e. greater than zero. Preferred enantioselective reactions
25 yield a product with an e.e. greater than 20%, more preferably greater than 50%, even more preferably greater than 70%, and most preferably greater than 80%.

A diastereoselective reaction converts a chiral reactant (which may be racemic or enantiomerically pure) to a product enriched in one diastereomer. If the chiral reactant is racemic, in the presence of a chiral non-racemic reagent or catalyst, one reactant enantiomer
30 may react more slowly than the other. This class of reaction is termed a kinetic resolution, wherein the reactant enantiomers are resolved by differential reaction rate to yield both enantiomerically-enriched product and enantiomerically-enriched unreacted substrate.

Kinetic resolution is usually achieved by the use of sufficient reagent to react with only one reactant enantiomer (i.e. one-half mole of reagent per mole of racemic substrate). Examples of catalytic reactions which have been used for kinetic resolution of racemic reactants include the Sharpless epoxidation and the Noyori hydrogenation.

5 A regioselective reaction is a reaction which occurs preferentially at one reactive center rather than another non-identical reactive center. For example, a regioselective reaction of an unsymmetrically substituted epoxide substrate would involve preferential reaction at one of the two epoxide ring carbons.

The term "non-racemic" with respect to the chiral catalyst, means a preparation of
10 catalyst having greater than 50% of a given enantiomer, more preferably at least 75%. "Substantially non-racemic" refers to preparations of the catalyst which have greater than 90% ee for a given enantiomer of the catalyst, more preferably greater than 95% ee.

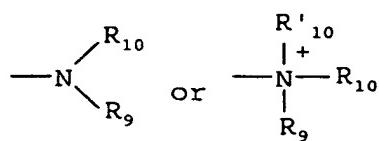
The term "alkyl" refers to the radical of saturated aliphatic groups, including straight-chain alkyl groups, branched-chain alkyl groups, cycloalkyl (alicyclic) groups, alkyl
15 substituted cycloalkyl groups, and cycloalkyl substituted alkyl groups. In preferred embodiments, a straight chain or branched chain alkyl has 30 or fewer carbon atoms in its backbone (e.g., C₁-C₃₀ for straight chain, C₃-C₃₀ for branched chain), and more preferably 20 or fewer. Likewise, preferred cycloalkyls have from 4-10 carbon atoms in their ring structure, and more preferably have 5, 6 or 7 carbons in the ring structure.

20 Unless the number of carbons is otherwise specified, "lower alkyl" as used herein means an alkyl group, as defined above, but having from one to ten carbons, more preferably from one to six carbon atoms in its backbone structure. Likewise, "lower alkenyl" and "lower alkynyl" have similar chain lengths.

The terms "alkenyl" and "alkynyl" refer to unsaturated aliphatic groups analogous in
25 length and possible substitution to the alkyls described above, but which contain at least one double or triple carbon-carbon bond, respectively.

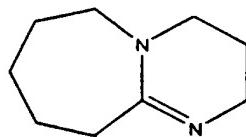
30 The term "organometallic" refers to compounds comprising a metallic atom (such as mercury, zinc, lead, magnesium or lithium) or a metalloid atom (such as silicon, or tin) that is bonded directly to a carbon atom, such as methyl magnesium bromide, phenyl lithium, and phenyl-trimethyl-tin.

The terms "amine" and "amino" are art-recognized and refer to both unsubstituted and substituted amines, e.g., a moiety that can be represented by the general formula:

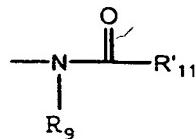


wherein R₉, R₁₀ and R'₁₀ each independently represent a group permitted by the rules of valence.

- The abbreviation "DBU" refers to 1,8-diazabicyclo[5.4.0]undec-7-ene, which has
5 the following structure:

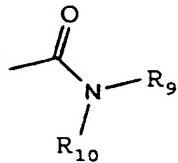


The term "acylamino" is art-recognized and refers to a moiety that can be represented by the general formula:



- 10 wherein R₉ is as defined above, and R'₁₁ represents a hydrogen, an alkyl, an alkenyl or -(CH₂)_m-R₈, where m and R₈ are as defined above.

The term "amido" is art recognized as an amino-substituted carbonyl and includes a moiety that can be represented by the general formula:



- 15 wherein R₉, R₁₀ are as defined above. Preferred embodiments of the amide will not include imides which may be unstable.

The term "alkylthio" refers to an alkyl group, as defined above, having a sulfur radical attached thereto. In preferred embodiments, the "alkylthio" moiety is represented by one of -S-alkyl, -S-alkenyl, -S-alkynyl, and -S-(CH₂)_m-R₈, wherein m and R₈ are defined above. Representative alkylthio groups include methylthio, ethyl thio, and the like.

The term "carbonyl" is art recognized and includes such moieties as can be represented by the general formula:

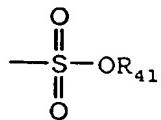


wherein X is a bond or represents an oxygen or a sulfur, and R₁₁ represents a hydrogen, an alkyl, an alkenyl, -(CH₂)_m-R_g or a pharmaceutically acceptable salt, R'₁₁ represents a hydrogen, an alkyl, an alkenyl or -(CH₂)_m-R_g, where m and R_g are as defined above.

- 5 Where X is an oxygen and R₁₁ or R'₁₁ is not hydrogen, the formula represents an "ester". Where X is an oxygen, and R₁₁ is as defined above, the moiety is referred to herein as a carboxyl group, and particularly when R₁₁ is a hydrogen, the formula represents a "carboxylic acid". Where X is an oxygen, and R'₁₁ is hydrogen, the formula represents a "formate". In general, where the oxygen atom of the above formula is replaced by sulfur,
- 10 the formula represents a "thiolcarbonyl" group. Where X is a sulfur and R₁₁ or R'₁₁ is not hydrogen, the formula represents a "thioester." Where X is a sulfur and R₁₁ is hydrogen, the formula represents a "thiolcarboxylic acid." Where X is a sulfur and R'₁₁ is hydrogen, the formula represents a "thiolformate." On the other hand, where X is a bond, and R₁₁ is not hydrogen, the above formula represents a "ketone" group. Where X is a bond, and R₁₁ is hydrogen, the above formula represents an "aldehyde" group.
- 15

The terms "alkoxyl" or "alkoxy" as used herein refers to an alkyl group, as defined above, having an oxygen radical attached thereto. Representative alkoxyl groups include methoxy, ethoxy, propyloxy, tert-butoxy and the like. An "ether" is two hydrocarbons covalently linked by an oxygen. Accordingly, the substituent of an alkyl that renders that alkyl an ether is or resembles an alkoxyl, such as can be represented by one of -O-alkyl, -O-alkenyl, -O-alkynyl, -O-(CH₂)_m-R_g, where m and R_g are described above.

The term "sulfonate" is art recognized and includes a moiety that can be represented by the general formula:



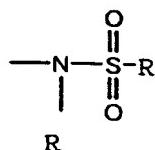
- 25 in which R₄₁ is an electron pair, hydrogen, alkyl, cycloalkyl, or aryl.

The terms triflyl, tosyl, mesyl, and nonaflyl are art-recognized and refer to trifluoromethanesulfonyl, p-toluenesulfonyl, methanesulfonyl, and nonafluorobutanesulfonyl groups, respectively. The terms triflate, tosylate, mesylate, and nonaflate are art-recognized and refer to trifluoromethanesulfonate ester, p-toluenesulfonate

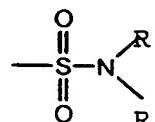
ester, methanesulfonate ester, and nonafluorobutanesulfonate ester functional groups and molecules that contain said groups, respectively.

The abbreviations Me, Et, Ph, Tf, Nf, Ts, Ms represent methyl, ethyl, phenyl, trifluoromethanesulfonyl, nonafluorobutanesulfonyl, *p*-toluenesulfonyl and methanesulfonyl, respectively. A more comprehensive list of the abbreviations utilized by organic chemists of ordinary skill in the art appears in the first issue of each volume of the *Journal of Organic Chemistry*; this list is typically presented in a table entitled Standard List of Abbreviations. The abbreviations contained in said list, and all abbreviations utilized by organic chemists of ordinary skill in the art are hereby incorporated by reference.

10 The term "sulfonylamino" is art recognized and includes a moiety that can be represented by the general formula:

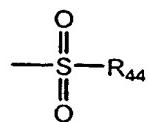


The term "sulfamoyl" is art-recognized and includes a moiety that can be represented by the general formula:



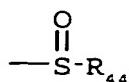
15

The term "sulfonyl", as used herein, refers to a moiety that can be represented by the general formula:



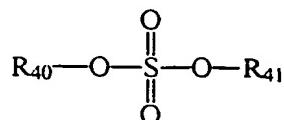
in which R₄₄ is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, 20 cycloalkyl, heterocyclyl, aryl, or heteroaryl.

The term "sulfoxido" as used herein, refers to a moiety that can be represented by the general formula:



in which R₄₄ is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aralkyl, or aryl.

The term "sulfate", as used herein, means a sulfonyl group, as defined above, attached to two hydroxy or alkoxy groups. Thus, in a preferred embodiment, a sulfate has the structure:



5

in which R₄₀ and R₄₁ are independently absent, a hydrogen, an alkyl, or an aryl. Furthermore, R₄₀ and R₄₁, taken together with the sulfonyl group and the oxygen atoms to which they are attached, may form a ring structure having from 5 to 10 members.

Analogous substitutions can be made to alkenyl and alkynyl groups to produce, for 10 example, alkenylamines, alkynylamines, alkenylamides, alkynylamides, alkenylimines, alkynylimines, thioalkenyls, thioalkynyls, carbonyl-substituted alkenyls or alkynyls, alkenoxyls, alkynoxyls, metalloalkenyls and metalloalkynyls.

The term "aryl" as used herein includes 4-, 5-, 6- and 7-membered single-ring aromatic groups which may include from zero to four heteroatoms, for example, benzene, 15 pyrrole, furan, thiophene, imidazole, oxazole, thiazole, triazole, pyrazole, pyridine, pyrazine, pyridazine and pyrimidine, and the like. Those aryl groups having heteroatoms in the ring structure may also be referred to as "aryl heterocycle". The aromatic ring can be substituted at one or more ring positions with such substituents as described above, as for example, halogens, alkyls, alkenyls, alkynyls, hydroxyl, amino, nitro, thiol amines, imines, 20 amides, phosphonates, phosphines, carbonyls, carboxyls, silyls, ethers, thioethers, sulfonyls, selenoethers, ketones, aldehydes, esters, or -(CH₂)_m-R₇, -CF₃, -CN, or the like.

The terms "heterocycle" or "heterocyclic group" refer to 4 to 10-membered ring structures, more preferably 5 to 7 membered rings, which ring structures include one to four heteroatoms. Heterocyclic groups include pyrrolidine, oxolane, thiolane, imidazole, 25 oxazole, piperidine, piperazine, morpholine. The heterocyclic ring can be substituted at one or more positions with such substituents as described above, as for example, halogens, alkyls, alkenyls, alkynyls, hydroxyl, amino, nitro, thiol, amines, imines, amides, phosphonates, phosphines, carbonyls, carboxyls, silyls, ethers, thioethers, sulfonyls, selenoethers, ketones, aldehydes, esters, or -(CH₂)_m-R₇, -CF₃, -CN, or the like.

The terms "polycycle" or "polycyclic group" refer to two or more cyclic rings (e.g., cycloalkyls, cycloalkenyls, cycloalkynyls, aryls and/or heterocycles) in which two or more carbons are common to two adjoining rings, e.g., the rings are "fused rings". Rings that are joined through non-adjacent atoms are termed "bridged" rings. Each of the rings of the

- 5 polycycle can be substituted with such substituents as described above, as for example, halogens, alkyls, alkenyls, alkynyls, hydroxyl, amino, nitro, thiol, amines, imines, amides, phosphonates, phosphines, carbonyls, carboxyls, silyls, ethers, thioethers, sulfonyls, selenoethers, ketones, aldehydes, esters, or $-(CH_2)_m-R_7$, $-CF_3$, $-CN$, or the like.

The term "heteroatom" as used herein means an atom of any element other than
10 carbon or hydrogen. Preferred heteroatoms are nitrogen, oxygen, sulfur, phosphorus and selenium.

For purposes of this invention, the chemical elements are identified in accordance with the Periodic Table of the Elements, CAS version, Handbook of Chemistry and Physics, 67th Ed., 1986-87, inside cover.

- 15 The terms *ortho*, *meta* and *para* apply to 1,2-, 1,3- and 1,4-disubstituted benzenes, respectively. For example, the names 1,2-dimethylbenzene and *ortho*-dimethylbenzene are synonymous.

The terms triflyl, tosyl, mesyl, and nonaflyl are art-recognized and refer to trifluoromethanesulfonyl, *p*-toluenesulfonyl, methanesulfonyl, and
20 nonafluorobutanesulfonyl groups, respectively. The terms triflate, tosylate, mesylate, and nonaflate are art-recognized and refer to trifluoromethanesulfonate ester, *p*-toluenesulfonate ester, methanesulfonate ester, and nonafluorobutanesulfonate ester functional groups and molecules that contain said groups, respectively.

The abbreviations Me, Et, Ph, Tf, Nf, Ts, and Ms, represent methyl, ethyl, phenyl,
25 trifluoromethanesulfonyl, nonafluorobutanesulfonyl, *p*-toluenesulfonyl and methanesulfonyl, respectively. A more comprehensive list of the abbreviations utilized by organic chemists of ordinary skill in the art appears in the first issue of each volume of the *Journal of Organic Chemistry*; this list is typically presented in a table entitled Standard List of Abbreviations. The abbreviations contained in said list, and all abbreviations utilized by organic chemists of ordinary skill in the art are hereby incorporated by reference.

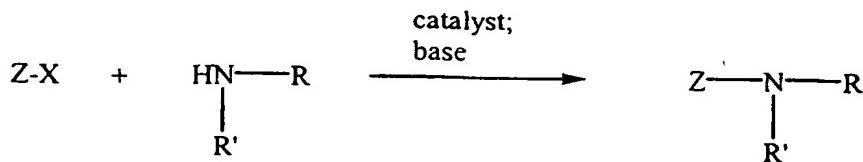
The phrase "protecting group" as used herein means temporary substituents which protect a potentially reactive functional group from undesired chemical transformations.

Examples of such protecting groups include esters of carboxylic acids, silyl ethers of alcohols, and acetals and ketals of aldehydes and ketones, respectively. The field of protecting group chemistry has been reviewed (Greene, T.W.; Wuts, P.G.M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, 1991).

- 5 As used herein, the term "substituted" is contemplated to include all permissible substituents of organic compounds. In a broad aspect, the permissible substituents include acyclic and cyclic, branched and unbranched, carbocyclic and heterocyclic, aromatic and nonaromatic substituents of organic compounds. Illustrative substituents include, for example, those described hereinabove. The permissible substituents can be one or more
 10 and the same or different for appropriate organic compounds. For purposes of this invention, the heteroatoms such as nitrogen may have hydrogen substituents and/or any permissible substituents of organic compounds described herein which satisfy the valencies of the heteroatoms. This invention is not intended to be limited in any manner by the permissible substituents of organic compounds.

15 Methods of the Invention

In certain embodiments, a method of the present invention is represented by Scheme 1:



Scheme 1

wherein

- 20 X represents I, Br, Cl, alkylsulfonate, or arylsulfonate;
 Z represents optionally substituted aryl, heteroaryl or alkenyl;
 catalyst comprises a copper atom or ion, and a ligand;
 base represents a Bronsted base;
 R represents alkyl, cycloalkyl, aralkyl, aryl, heteroaryl, formyl, acyl, alkylO₂C-,
 25 aryI O₂C-, heteroaryI O₂C-, aralkylO₂C-, heteroaralkylO₂C-, acyl(R')N-, alkylOC(O)N(R')-,
 aryI OC(O)N(R')-, aralkylOC(O)N(R')-, heteroaralkylOC(O)N(R')-, -N=C(alkyl)₂, or
 N=C(aryl)₂;

R' represents H, alkyl, cycloalkyl, aralkyl, heteroaralkyl, aryl, heteroaryl, formyl, acyl, amino, or -C(NR'')N(R'')₂;

R'' represents independently for each occurrence H, alkyl, cycloalkyl, aryl, heteroaryl, aralkyl or heteroaralkyl;

5 R and R' taken together may represent =C(alkyl)₂, or =C(aryl)₂; and

R and R' are optionally connected by a covalent bond;

provided that when R is aryl or heteroaryl, R' is not formyl or acyl;

further provided that when R is formyl or acyl, R' is not aryl or heteroaryl.

10 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br.

15 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

20 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

25 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol; 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the ligand comprised by the catalyst is a chelating ligand.

- In certain embodiments, the methods of the present invention are represented by
- 5 Scheme 1 and the attendant definitions, wherein the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the ligand comprised by the catalyst is cis-10 1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-15 dimethyl-1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- 25 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the catalyst is present in less than or equal 30 to about 10 mol% relative to Z-X.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the catalyst is present in less than or equal to about 5 mol% relative to Z-X.

5 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the catalyst is present in less than or equal to about 1 mol% relative to Z-X.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the catalyst is present in less than or equal to about 0.1 mol% relative to Z-X.

10 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the method is conducted at a temperature less than about 150 C.

15 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the method is conducted at a temperature less than about 140 C.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the method is conducted at a temperature less than about 110 C.

20 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the method is conducted at a temperature less than about 100 C.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the method is conducted at a temperature less than about 90 C.

25 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the *~~peB6dX~~ is conducted at a temperature less than about 50 C.

30 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the method is conducted at a temperature less than about 40 C.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein the method is conducted at ambient temperature.

5 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein Z represents optionally substituted aryl.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein Z represents optionally substituted phenyl.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein R' represents H, or alkyl.

10 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

15 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

20 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

25 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is a chelating ligand.

30 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; and the ligand comprised by

the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-

(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and

5 the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, 10 alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, 15 hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, 25 or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate,

phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-

hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-

- (dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-
5 (dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is a chelating ligand.

- In certain embodiments, the methods of the present invention are represented by
10 Scheme 1 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br; and the ligand comprised
15 by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane,
20 ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- 5 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-
10 (dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and
15 the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- 20 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

25 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane,

ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- In certain embodiments, the methods of the present invention are represented by
- 5 Scheme 1 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or
10 guanidine.

- In certain embodiments, the methods of the present invention are represented by
- Scheme 1 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-
15 aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

- In certain embodiments, the methods of the present invention are represented by
- Scheme 1 and the attendant definitions, wherein X represents Br; the ligand comprised by
20 the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

- In certain embodiments, the methods of the present invention are represented by
- Scheme 1 and the attendant definitions, wherein X represents Br; the ligand comprised by
25 the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-
30 phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and

the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 5

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 10

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
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- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 25

- 30 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; and the ligand comprised

by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; and the ligand comprised
- 5 by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; and the ligand comprised
- by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol,
- 10 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.
- 15

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; and the ligand comprised
- by the catalyst is a chelating ligand.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; and the ligand comprised
- 20
- by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; and the ligand comprised
- 25
- by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane,
- 30 ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; and the ligand comprised

by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

- 5 In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, 10 fluoride, or guanidine.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, 15 aryloxide, amine, metal amide, fluoride, or guanidine.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 20 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and 25 the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, 30 alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; the ligand comprised by

the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- In certain embodiments, the methods of the present invention are represented by
- 5 Scheme 1 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 10

- In certain embodiments, the methods of the present invention are represented by
- 15 Scheme 1 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 20

- In certain embodiments, the methods of the present invention are represented by
- Scheme 1 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 25

- In certain embodiments, the methods of the present invention are represented by
- Scheme 1 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 30

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and

5 the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

10 the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate,

15 cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

20

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or

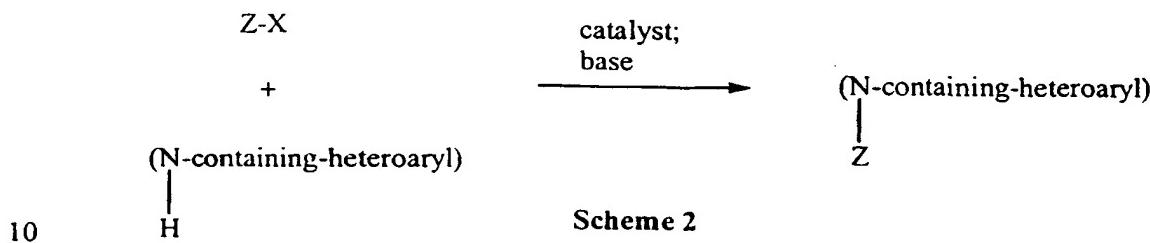
25

30 sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 1 and the attendant definitions, wherein X represents Cl; the ligand comprised by

the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, a method of the present invention is represented by Scheme 2:



Scheme 2

wherein

X represents I, Br, Cl, alkylsulfonate, or arylsulfonate:

Z represents optionally substituted aryl, heteroaryl or alkenyl:

(N-containing-heteroaryl)-H represents optionally substituted pyrazole, pyrrole,

15 tetrazole, imidazole, indazole, 1,2,3-triazole, 1,2,4-trizole, indole, carbazole, benzotriazole, benzimidazole, guanine, purine, adenine, xanthine, 8-azaadenine, 8-azoapoxanthine, uracil, 6-azauracil, cytosine, thymine, 6-azathymine, uric acid, benzoylene urea, 4-(3*H*)-pyrimidone, pyridone, 1(2*H*)-phthalazinone, 1,2,3-benzotriazine-4(3*H*)-one, benzimidazolinone, 2-benzoxazolinone, thymidine, uridine, (-)-inosine, 1*H*-1,2,3,5-diazadiphosphole, 1*H*-1,2,3-azadiphosphole, 1*H*-1,2,4-azadiphosphole, 1*H*-1,2,4-diazaphosphole, 1*H*-1,2,3-diazaphosphole, 1*H*-1,3,2-diazaphosphole, 1*H*-1,2-azadiphosphole, 1*H*-1,3-azadiphosphole, 1*H*-1,2,3,4-triazaphosphole, 1*H*-1,2,3,5-dithiadiazolidene, 1*H*-1,3,2,4-dithiadiazolidene, 1,3,2-oxathiazole, 3*H*-1,2,3-oxathiazole, 1,3,2-dithiazole, 1*H*-1,2-azaborole, pentazole, 3*H*-1,2,3-dioxazole, 2*H*-1,2,3-oxadiazine, 25 2*H*-1,2,4-oxadiazine, 2*H*-1,2,5-oxadiazine, 2*H*-1,2,6-oxadiazine, 2*H*-1,2,3-thiadiazine, 2*H*-1,2,4-thiadiazine, 2*H*-1,2,5-thiadiazine, 2*H*-1,2,6-thiadiazine, 2*H*-1,2-thiazine, 1,3,5,2,4,6-trithiatriazine, 2*H*-1,2,4,5-oxatriazine, 4*H*-1,3,2,4-dithiadiazine, 2*H*, 4*H*-1,3,2,5-dioxadiazine, 2*H*-1,5,2,4-dioxadiazine, 2*H*-1,2,4,6-thiatriazine, 2*H*-1,2,4,5-thiatriazine, 4*H*-

- 1,3,2-dithiazane, 4H-1,3,2-dioxazine, 2H-1,5,2-dioxazine, 1,3,4-dithiazane, 4H-1,3,2-
oxathiazine, 2H,4H-1,3,2-oxathiazine, 2H, 4H-1,5,2-oxathiazine, 2H-1,2-diazepine, 2H-1,3-
diazepine, 2H-1,4-diazepine, 2H-1,2,5-triazepine, 2H-1,3,5-triazepine, 2H-1,2,4-triazepine,
1H-azepine, 2H-1,2,3,5-tetrazepine, 2H-1,2,4,6-tetrazepine, 2H-1,2,4,5-tetrazepine, 2H-
5 1,5,2,4-dithiadiazepine, 1,3,5,2,4,7-trithiatriazepine, 1,3,5,2,4-trithiadiazepine, pentahydro-
1,3,5,2,4,6,8-trithiatetrazocene, 2H,6H-1,5,2,4,6,8-dithiatetrazocene, 2H-1,2,5-oxadiazocine,
2H-1,2,6-oxadiazocine, 2H-1,2-oxazocine, 2H-1,2-thiazocine, 4H-1,2,5-thiadiazocine, 4H-
1,2,6-thiadiazocine, 5H-[1,2,4]-thiadiazolo[1,5-b][1,2,4]oxathiazole, triazolothiadiazole,
thienothiadiazole, 1H-imidazo[1,2-a]imidazole, 4H-furo[3,2-b]pyrrole[3,4-b], 1H-
10 pyrrolopyrazole, 1H-[2,3-d]thienopyrazole, 1H-[3,4-d]thienopyrazole, 1H-[2,3-
c]thienopyrazole, 1H-[3,4-c]thienopyrazole, 1H-1,3-benzazaphole, 1H-benzazepine, 2H-2-
benzazepine, 1H-1,3-benzodiazepine, 1H-1,4-benzodiazepine, 1H-1,5-benzodiazepine, 1H-
1,2,4-benzotriazepine, 1H-1,2,5-benzotriazepine, 1H-1,3,4-benzotriazepine, or 3H-3-
benzazepine;
15 catalyst comprises a copper atom or ion, and a ligand; and
base represents a Bronsted base.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein (N-containing-heteroaryl)-H represents optionally substituted pyrrole, pyrazole, indole, indazole, azaindole, carbazole, imidazole, purine, or benzimidazole.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Cl.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

- In certain embodiments, the methods of the present invention are represented by
- 5 Scheme 2 and the attendant definitions, wherein the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline,
- 10 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

- In certain embodiments, the methods of the present invention are represented by
- Scheme 2 and the attendant definitions, wherein the ligand comprised by the catalyst is a
- 15 chelating ligand.

- In certain embodiments, the methods of the present invention are represented by
- Scheme 2 and the attendant definitions, wherein the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.
- 20 In certain embodiments, the methods of the present invention are represented by
- Scheme 2 and the attendant definitions, wherein the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane,
- 25 cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by
- Scheme 2 and the attendant definitions, wherein the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-

diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein the base is a carbonate, phosphate, oxide, 5 hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by 10 Scheme 2 and the attendant definitions, wherein the catalyst is present in less than or equal to about 10 mol% relative to Z-X.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein the catalyst is present in less than or equal to about 5 mol% relative to Z-X.

15 In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein the catalyst is present in less than or equal to about 1 mol% relative to Z-X.

In certain embodiments, the methods of the present invention are represented by 20 Scheme 2 and the attendant definitions, wherein the catalyst is present in less than or equal to about 0.1 mol% relative to Z-X.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein the method is conducted at a temperature less than about 150 C.

In certain embodiments, the methods of the present invention are represented by 25 Scheme 2 and the attendant definitions, wherein the method is conducted at a temperature less than about 140 C.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein the method is conducted at a temperature less than about 110 C.

30 In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein the method is conducted at a temperature less than about 100 C.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein the method is conducted at a temperature less than about 90 C.

5 In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein the method is conducted at a temperature less than about 50 C.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein the method is conducted at a temperature less than about 40 C.

10 In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein the method is conducted at ambient temperature.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein Z represents optionally substituted aryl.

15 In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein Z represents optionally substituted phenyl.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

25 In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-

30 (dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-

phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; and the ligand comprised by 5 the catalyst is a chelating ligand.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

10 In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-
15 diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; and the ligand comprised by 20 the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

25 In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

30 In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane;

and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- In certain embodiments, the methods of the present invention are represented by
- 10 Scheme 2 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 15 In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 20 In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 25 In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; the ligand comprised by the

catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; and the ligand comprised

by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

- In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

- In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is a chelating ligand.

- In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base 5 is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine. 10

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine; and (methylimino)diacetic acid; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine. 15 20

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine. 25

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine. 30

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-

isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-
5 phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by
10 Scheme 2 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by
15 Scheme 2 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by
20 Scheme 2 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane,
25 ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by
30 Scheme 2 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-

diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

- In certain embodiments, the methods of the present invention are represented by
5 Scheme 2 and the attendant definitions, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

- In certain embodiments, the methods of the present invention are represented by
Scheme 2 and the attendant definitions, wherein X represents Cl; and the ligand comprised
10 by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

- In certain embodiments, the methods of the present invention are represented by
Scheme 2 and the attendant definitions, wherein X represents Cl; and the ligand comprised
by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol,
15 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-
20 (dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

In certain embodiments, the methods of the present invention are represented by
Scheme 2 and the attendant definitions, wherein X represents Cl; and the ligand comprised
by the catalyst is a chelating ligand.

- In certain embodiments, the methods of the present invention are represented by
25 Scheme 2 and the attendant definitions, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by
Scheme 2 and the attendant definitions, wherein X represents Cl; and the ligand comprised
30 by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-

diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by
- 5 Scheme 2 and the attendant definitions, wherein X represents Cl; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.
- 10 In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, 15 fluoride, or guanidine.

- In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, 20 fluoride, or guanidine.

- In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 25 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and 30 the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

5 In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

10 In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-

15 diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

20 In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-

25 diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base

is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Cl; the ligand comprised by 5 the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Cl; the ligand comprised by 10 the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-15 phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by 20 Scheme 2 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

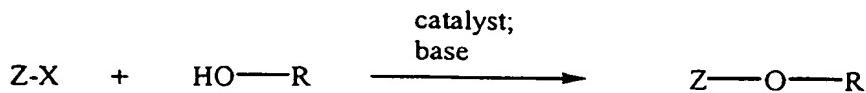
In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Cl; the ligand comprised by 25 the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Cl; the ligand comprised by 30 the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-

diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 2 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, a method of the present invention is represented by Scheme 3:



Scheme 3

wherein

X represents I, Br, Cl, alkylsulfonate, or arylsulfonate;

Z represents optionally substituted aryl, heteroaryl, or alkenyl;

catalyst comprises a copper atom or ion, and a ligand;

base represents a Bronsted base; and

R represents optionally substituted alkyl, cycloalkyl, aralkyl, heteroaralkyl, alkenylalkyl, or alkynylalkyl.

25

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Br.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Cl.

5 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

10 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

15 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline; 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

20 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the ligand comprised by the catalyst is a chelating ligand.

25 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

30 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane,

cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by
- 5 Scheme 3 and the attendant definitions, wherein the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.
- 10 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the base is potassium phosphate, potassium 15 carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the catalyst is present in less than or equal to about 10 mol% relative to Z-X.
- In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the catalyst is present in less than or equal 20 to about 5 mol% relative to Z-X.
- In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the catalyst is present in less than or equal to about 1 mol% relative to Z-X.
- 25 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the catalyst is present in less than or equal to about 0.1 mol% relative to Z-X.
- In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the method is conducted at a temperature 30 less than about 150 C.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the method is conducted at a temperature less than about 140 C.

5 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the method is conducted at a temperature less than about 110 C.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the method is conducted at a temperature less than about 100 C.

10 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the method is conducted at a temperature less than about 90 C.

15 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the method is conducted at a temperature less than about 50 C.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the method is conducted at a temperature less than about 40 C.

20 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein the method is conducted at ambient temperature.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein Z represents optionally substituted aryl.

25 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein Z represents optionally substituted phenyl.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

30 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; and the ligand comprised by

the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

- In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

- In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is a chelating ligand.

- 15 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

- 16 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

- 17 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base 5 is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; 10 and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-20 (dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-

isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-

diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

- In certain embodiments, the methods of the present invention are represented by
- 5 Scheme 3 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

- In certain embodiments, the methods of the present invention are represented by
- Scheme 3 and the attendant definitions, wherein X represents Br; and the ligand comprised
- 10 by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

- In certain embodiments, the methods of the present invention are represented by
- Scheme 3 and the attendant definitions, wherein X represents Br; and the ligand comprised
- by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol,
- 15 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.
- 20

In certain embodiments, the methods of the present invention are represented by

Scheme 3 and the attendant definitions, wherein X represents Br; and the ligand comprised

by the catalyst is a chelating ligand.

- In certain embodiments, the methods of the present invention are represented by
- 25 Scheme 3 and the attendant definitions, wherein X represents Br; and the ligand comprised
- by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by
- Scheme 3 and the attendant definitions, wherein X represents Br; and the ligand comprised
- 30 by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-

diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by
- 5 Scheme 3 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.
- 10 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, 15 fluoride, or guanidine.
- In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, 20 aryloxide, amine, metal amide, fluoride, or guanidine.
- In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 25 (dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and 30 the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- 5 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 10 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-
- 15 diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 20 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-
- 25 diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base

is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-

5 diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

10 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

15 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

20 In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Cl; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Cl; and the ligand comprised by the catalyst is a chelating ligand.

- In certain embodiments, the methods of the present invention are represented by
- 5 Scheme 3 and the attendant definitions, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by
- Scheme 3 and the attendant definitions, wherein X represents Cl; and the ligand comprised
- 10 by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane,
- 15 ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by
- Scheme 3 and the attendant definitions, wherein X represents Cl; and the ligand comprised
- by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-
- 20 N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by
- Scheme 3 and the attendant definitions, wherein X represents Cl; the ligand comprised by
- the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-
- 25 aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base
- is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide,
- fluoride, or guanidine.

- In certain embodiments, the methods of the present invention are represented by
- Scheme 3 and the attendant definitions, wherein X represents Cl; the ligand comprised by
- 30 the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-
5 (dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and
10 the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide,
15 alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide,
20 hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-
25 dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride,
30 or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Cl; the ligand comprised by

the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, 5 phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-10 aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Cl; the ligand comprised by 15 the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Cl; the ligand comprised by 20 the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-25 phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

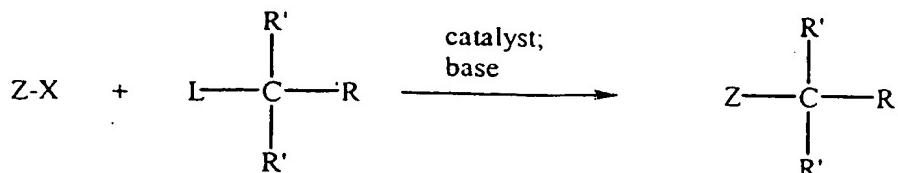
In certain embodiments, the methods of the present invention are represented by 30 Scheme 3 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 3 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, a method of the present invention is represented by Scheme 4:



Scheme 4

wherein

X represents I, Br, Cl, alkylsulfonate, or arylsulfonate;
Z represents optionally substituted aryl, heteroaryl or alkenyl;
L represents H or a negative charge;
catalyst comprises a copper atom or ion, and a ligand;
5 base represents a Bronsted base;
R represents H, optionally substituted alkyl, cycloalkyl, aralkyl, aryl, or heteroaryl;
R' represents independently for each occurrence H, alkyl, cycloalkyl, aralkyl, aryl, or
heteroaryl, formyl, acyl, -CO₂R'', -C(O)N(R)₂, sulfonyl, -P(O)(OR'')₂, -CN, or -NO₂;
R'' represents independently for each occurrence optionally substituted alkyl,
10 cycloalkyl, aralkyl, aryl, or heteroaryl; and
C(R')₂(R) taken together may represent nitrile.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I.
15 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br.
In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl.
20 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.
In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the ligand comprised by the catalyst is an
optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.
25 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 30 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-

phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the ligand comprised by the catalyst is a chelating ligand.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

10 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane,

15 cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

20 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

25 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

~ In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

30 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the catalyst is present in less than or equal to about 10 mol% relative to Z-X.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the catalyst is present in less than or equal to about 5 mol% relative to Z-X.

5 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the catalyst is present in less than or equal to about 1 mol% relative to Z-X.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the catalyst is present in less than or equal to about 0.1 mol% relative to Z-X.

10 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the method is conducted at a temperature less than about 150 C.

15 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the method is conducted at a temperature less than about 140 C.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the method is conducted at a temperature less than about 110 C.

20 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the method is conducted at a temperature less than about 100 C.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the method is conducted at a temperature less than about 90 C.

25 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the method is conducted at a temperature less than about 50 C.

30 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the method is conducted at a temperature less than about 40 C.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein the method is conducted at ambient temperature.

In certain embodiments, the methods of the present invention are represented by
5 Scheme 4 and the attendant definitions, wherein Z represents optionally substituted aryl.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein Z represents optionally substituted phenyl.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein R represents H.

10 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein R' represents independently for each occurrence acyl, or -CO₂R".

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein R" represents independently for each 15 occurrence alkyl, cycloalkyl, or aralkyl.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

20 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

In certain embodiments, the methods of the present invention are represented by
25 Scheme 4 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 30 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is a chelating ligand.

- In certain embodiments, the methods of the present invention are represented by
- 5 Scheme 4 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; and the ligand comprised by
- 10 the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane,
- 15 ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

- In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-

5 (dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and

10 the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; the ligand comprised by the

catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, 5 phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide. 10

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; 15 and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide. 20 25

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide. 30

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-

5 (dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

10 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is a chelating ligand.

15 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

20 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

25 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

30 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; the ligand comprised by

the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

5 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide,

aryloxide, amine, metal amide, fluoride, or guanidine.

10 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-

15 (dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

25 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

30 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis-

and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane,
5 ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; the ligand comprised by
10 the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or
15 guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base
20 is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
25

• In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline,
30

4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

5 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

10 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

15 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

20 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

5 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

In certain embodiments, the methods of the present invention are represented by
10 Scheme 4 and the attendant definitions, wherein X represents Cl; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline,
15 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; and the ligand comprised by the catalyst is a chelating ligand.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

25 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-
5 N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-
10 aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-
15 diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-
20 isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-
25 phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and
the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal
amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- 5 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-
10 dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride,
15 or guanidine.

- In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-
20 dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

- 25 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

- 30 In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-

diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

- In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

- In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

- In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

- In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

In certain embodiments, the methods of the present invention are represented by Scheme 4 and the attendant definitions, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

Catalysts of the Invention

10 In general, the catalysts used in the methods of the present invention comprise a copper atom or ion, and a ligand. The copper atom or ion of the catalyst may be derived from any commercially available copper salt, e.g., a copper (I) or copper (II) salt. In certain embodiments, the copper atom or ion is provided as copper (I) iodide.

15 The ligand of a catalyst comprises a Lewis basic atom, e.g., selected from nitrogen, oxygen, sulfur, phosphorus, and arsenic, such that the Lewis basic atom is capable of interacting with the aforementioned copper atom or ion. The ligand of a catalyst may be a chelating ligand, i.e., a ligand comprising two Lewis basic atoms, e.g., selected from nitrogen, oxygen, phosphorus, and arsenic, with a spatial relationship therebetween, such that the Lewis basic atoms are capable of interacting simultaneously with the
20 aforementioned copper atom or ion. For example, a chelating ligand may be a diamine, aminoalcohol, or a bis-phosphine. In certain embodiments, a chelating ligand is a 1,2-diamine, or 1,3-diamine. In certain embodiments, a chelating ligand is a 1,2-diaminocyclohexane, a 1,10-phenanthroline, a 2-hydroxyethyl amine, or a 1,2-diaminoethane. In certain embodiments, a chelating ligand is 1,2-diaminocyclohexane,
25 N,N'-dimethyl-1,2-diaminocyclohexane, N-tolyl-1,2-diaminocyclohexane, 1,10-phenanthroline, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane. In certain embodiments, a chelating ligand is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, or a mixture of cis- and trans-1,2-diaminocyclohexane. Additionally, with respect to asymmetric chelating ligands, the ligand may be provided as a single
30 enantiomer, a mixture of stereoisomers, or a racemic mixture. In certain embodiments, the ligand serves as the solvent for a method of the present invention. For example, in an embodiment wherein the ligand comprised by the catalyst is an amine that is a liquid under

the conditions for practicing a method of the present invention, the method may be practiced using said amine as the solvent.

The copper atom or ion and the ligand of the catalyst of the methods of the present invention may be added to the reaction mixture separately or simultaneously, or they may be
5 added in the form of preformed catalyst complex. Although the methods of the present invention do not require the formation of a copper-chelating ligand complex, such complexes are likely present. Moreover, the identity of the ligand effects various characteristics of the methods of the present invention.

In certain embodiments, the catalyst of a method of the present invention is
10 covalently tethered to a solid support, e.g., a polymer bead or a resin. For example, the ligand of a catalyst of the present invention may be covalently tethered to a solid support, e.g., a Wang resin. Additionally, one or more of the substrates of a method of the present invention may be covalently tethered to a solid support, e.g., a polymer bead or a resin. For example, the Z-X substrate of a method of the present invention may be covalently tethered
15 to a solid support, e.g., a Wang resin. Alternatively, the nucleophilic substrate, i.e., the substrate that effectively replaces X in Z-X, of a method of the present invention may be covalently tethered to a solid support, e.g., a Wang resin. Further, in certain embodiments, both substrates may be covalently tethered to a solid support. In certain embodiments, one or more of the substrates or the catalyst or any of them are isolated in a semi-permeable
20 membrane, e.g., a dialysis bag.

Suitable Bases

A wide range of Bronsted bases may be used in the methods of the present invention. Generally, any Bronsted base may be used in the methods of the present invention. For example, suitable bases include K₃PO₄, K₂CO₃, Na₂CO₃, Tl₂CO₃, Cs₂CO₃,
25 K(O/Bu), Li(O/Bu), Na(O/Bu), K(OPh), and Na(OPh), or mixtures thereof. In certain embodiments, the Bronsted base used will be selected from the group consisting of phosphates, carbonates, and alkoxides. In certain embodiments, the base is selected from the group consisting of potassium phosphate, potassium carbonate, cesium carbonate, and sodium *tert*-butoxide.

30 Typically, there is no need to use large excesses of base in the methods of the present invention. In certain embodiments, no more than four equivalents of base are used, relative to the nucleophilic reactant. In other embodiments, no more than two equivalents

of base are used, relative to the nucleophilic reactant. Further, in reactions using the corresponding anion of the nucleophilic reactant in place of its conjugate base, there may be no need for additional base.

Nucleophiles

- 5 Nucleophiles which are useful in the methods of the present invention may be selected by the skilled artisan according to several criteria. In general, a suitable nucleophile will have one or more of the following properties: 1) It will be capable of reaction with the substrate at the desired electrophilic site; 2) It will yield a useful product upon reaction with the substrate; 3) It will not react with the substrate at functionalities
10 other than the desired electrophilic site; 4) It will react with the substrate at least partly through a mechanism catalyzed by the chiral catalyst; 5) It will not substantially undergo further undesired reaction after reacting with the substrate in the desired sense; and 6) It will not substantially react with or degrade the catalyst. It will be understood that while undesirable side reactions (such as catalyst degradation) may occur, the rates of such
15 reactions can be rendered slow -- through the selection of reactants and conditions -- in comparison with the rate of the desired reaction(s).

Routine experimentation may be necessary to determine the preferred nucleophile for a given transformation. For example, if a nitrogen-containing nucleophile is desired, in order to form a carbon-nitrogen bond, it may be selected from the group comprising amines, amides, and imides. Further, heteroaromatics may also be used as the nucleophilic reactant.
20 For example, a carbon-nitrogen bond may be formed comprising the nitrogen of an optionally substituted indole, pyrrole, or carbazole. Moreover, numerous other nitrogen-containing functional groups serve as substrates in the instant methods of forming carbon-nitrogen bonds. For example, hydrazines, acylhydrazines, hydrazone, imines, and
25 alkoxy carbonylhydrazines are suitable substrates for the carbon-nitrogen bond-forming methods of the present invention.

- Similarly, an oxygen-containing nucleophile, such as an alcohol, alkoxide, or siloxane, may be used to form an oxygen-carbon bond; and a sulfur-containing nucleophile, such as a mercaptan, may be used to form a carbon-sulfur bond. Likewise, a carbon
30 nucleophile, e.g., a malonate or a beta-keto ester, may be used to form a carbon-carbon bond. Additional suitable nucleophiles will be apparent to those of ordinary skill in the art of organic chemistry. A nucleophile introduced in the reaction mixture as an anion may

comprise a conventional counterion, e.g., an alkali metal cation, alkaline earth cation, or ammonium ion. In certain embodiments, the nucleophilic moiety may be part of the substrate, resulting in an intramolecular bond-forming reaction.

In certain embodiments, the nucleophile is selected from the group consisting of
5 primary amides, secondary amides, lactams, hydrazines, imines, hydrazone, carbazates, primary amines, secondary amines, NH-containing heteroaromatics (e.g., pyrroles, indoles, and imidazoles), malonates, carbamates, imides, and alcohols.

Aryl, Heteroaryl or Vinyl Halides or Sulfonates

The methods of the present invention may be used to form a bond between the
10 halogen-bearing or sulfonate-bearing carbon atom of an aryl halide or sulfonate, heteroaryl halide or sulfonate, or vinyl halide or sulfonate, and a nucleophilic nitrogen or carbon or oxygen atom of a second molecule. Of course, as mentioned *supra*, the halogen-bearing carbon of the aryl halide, heteroaryl halide, or vinyl halide, or the sulfonate-bearing carbon of the aryl sulfonate, heteroaryl sulfonate, or vinyl sulfonate, and the nucleophilic nitrogen or carbon may be part of a single molecule, rendering the bond-formation intramolecular.
15

In certain embodiments, an aryl halide or sulfonate is used, wherein its aryl moiety is a radical of an aromatic hydrocarbon (single or polycyclic), such as benzene, naphthalene, anthracene and phenanthrene. In certain embodiments, the aryl halide may be selected from the group consisting of optionally-substituted phenyl halides.

20 In certain embodiments, a heteroaryl halide or sulfonate is used, wherein its heteroaryl moiety is a radical of an heteroaromatic (single or polycyclic), such as pyrrole, thiophene, thianthrene, furan, pyran, isobenzofuran, chromene, xanthene, phenoxathiin, pyrrole, imidazole, pyrazole, thiazole, isothiazole, isoxazole, pyridine, pyrazine, pyrimidine, pyridazine, indolizine, isoindole, indole, indazole, purine, quinolizine, isoquinoline,
25 quinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, carbazole, carboline, phenanthridine, acridine, perimidine, phenanthroline, phenazine, phenarsazine, phenothiazine, furazan, phenoxazine, pyrrolidine, oxolane, thiolane, oxazole, piperidine, piperazine, morpholine.

30 In general, suitable aromatic compounds have the formula Z_pArX , wherein Ar is aryl or heteroaryl; and X is a sulfonate or a halogen selected from the group consisting of chlorine, bromine, and iodine. In certain embodiments, X is a halide selected from the group consisting of chlorine, bromine, and iodine. In certain embodiments, X represents a

sulfonate moiety. Further, Z represents one or more optional substituents on the aromatic ring, though each occurrence of Z ($p > 1$) is independently selected. By way of example only, each incidence of substitution independently can be, as valence and stability permit, a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl (e.g., an ester, a 5 carboxylate, or a formate), a thiocarbonyl (e.g., a thioester, a thiolcarboxylate, or a thiolformate), an aldehyde, an amino, an acylamino, an amido, an amidino, a cyano, a nitro, an azido, a sulfonyl, a sulfoxido, a sulfate, a sulfonate, a sulfamoyl, a sulfonamido, a phosphoryl, a phosphonate, a phosphinate, $-(CH_2)_m-R_8$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$ -lower alkyl, $-(CH_2)_m-O$ -lower alkenyl, $-(CH_2)_m-O-(CH_2)_n-R_8$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$ -lower 10 alkyl, $-(CH_2)_m-S$ -lower alkenyl, $-(CH_2)_m-S-(CH_2)_n-R_8$, or protecting groups of the above or a solid or polymeric support; R₈ represents a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle; and n and m are independently for each occurrence zero or an integer in the range of 1 to 6. When the aryl moiety is phenyl, p is in the range of 0 to 5. For fused rings, where the number of potential substitution sites on the aryl moiety 15 is greater than five, the range defined for p must be adjusted appropriately.

Reaction Conditions

The methods of the present invention may be performed under a wide range of conditions, though it will be understood that the solvents and temperature ranges recited herein are not limitative and only correspond to a preferred mode of the process of the 20 invention.

In general, it will be desirable that reactions are run using mild conditions which will not adversely affect the reactants, the catalyst, or the product. For example, the reaction temperature influences the speed of the reaction, as well as the stability of the reactants, products and catalyst.

25 In certain embodiments, the methods of the present invention are conducted at a temperature less than about 150 C. In certain embodiments, the methods of the present invention are conducted at a temperature less than about 140 C. In certain embodiments, the methods of the present invention are conducted at a temperature less than about 110 C. In certain embodiments, the methods of the present invention are conducted at a temperature less than about 100 C. In certain embodiments, the methods of the present invention are conducted at a temperature less than about 90 C. In certain embodiments, the methods of the present invention are conducted at a temperature less than about 50 C. In 30

certain embodiments, the methods of the present invention are conducted at a temperature less than about 40 C. In certain embodiments, the methods of the present invention are conducted at ambient temperature.

In general, the subject reactions are carried out in a liquid reaction medium. The 5 reactions may be run without addition of solvent. Alternatively, the reactions may be run in an inert solvent, preferably one in which the reaction ingredients, including the catalyst, are substantially soluble. Suitable solvents include ethers such as diethyl ether, 1,2-dimethoxyethane, diglyme, t-butyl methyl ether, tetrahydrofuran and the like; halogenated solvents such as chloroform, dichloromethane, dichloroethane, chlorobenzene, and the like; 10 aliphatic or aromatic hydrocarbon solvents such as benzene, xylene, toluene, hexane, pentane and the like; esters and ketones such as ethyl acetate, acetone, and 2-butanone; polar aprotic solvents such as acetonitrile, dimethylsulfoxide, dimethylformamide and the like; or combinations of two or more solvents.

The invention also contemplates reaction in a biphasic mixture of solvents, in an 15 emulsion or suspension, or reaction in a lipid vesicle or bilayer. In certain embodiments, it may be preferred to perform the catalyzed reactions in the solid phase with one of the reactants anchored to a solid support.

In certain embodiments it is preferable to perform the reactions under an inert atmosphere of a gas such as nitrogen or argon.

20 The reaction processes of the present invention can be conducted in continuous, semi-continuous or batch fashion and may involve a liquid recycle operation as desired. The processes of this invention are preferably conducted in batch fashion. Likewise, the manner or order of addition of the reaction ingredients, catalyst and solvent are also not generally critical to the success of the reaction, and may be accomplished in any 25 conventional fashion.

The reaction can be conducted in a single reaction zone or in a plurality of reaction zones, in series or in parallel or it may be conducted batchwise or continuously in an elongated tubular zone or series of such zones. The materials of construction employed should be inert to the starting materials during the reaction and the fabrication of the 30 equipment should be able to withstand the reaction temperatures and pressures. Means to introduce and/or adjust the quantity of starting materials or ingredients introduced batchwise or continuously into the reaction zone during the course of the reaction can be

conveniently utilized in the processes especially to maintain the desired molar ratio of the starting materials. The reaction steps may be effected by the incremental addition of one of the starting materials to the other. Also, the reaction steps can be combined by the joint addition of the starting materials to the metal catalyst. When complete conversion is not desired or not obtainable, the starting materials can be separated from the product and then recycled back into the reaction zone.

The processes may be conducted in either glass lined, stainless steel or similar type reaction equipment. The reaction zone may be fitted with one or more internal and/or external heat exchanger(s) in order to control undue temperature fluctuations, or to prevent any possible "runaway" reaction temperatures.

Furthermore, one or more of the reactants or the catalyst can be immobilized by attachment to or incorporation into a polymer or other insoluble matrix.

Subsequent Transformations

A product synthesized by a method of the present invention may be either an end-product or an intermediate in a synthesis scheme. In cases where the product synthesized by a method of the present invention is an intermediate, the product may be subjected to one or more additional transformations to yield the desired end-product. The set of additional transformations contemplated comprises isomerizations, hydrolyses, oxidations, reductions, additions, eliminations, olefinations, functional group interconversions, transition metal-mediated reactions, transition metal-catalyzed reactions, bond-forming reactions, cleavage reactions, fragmentation reactions; thermal reactions, photochemical reactions, cycloadditions, sigmatropic rearrangements, electrocyclic reactions, chemoselective reactions, regioselective reactions, stereoselective reactions, diastereoselective reactions, enantioselective reactions, and kinetic resolutions. The invention expressly comprises use of a method of the present invention as a step -- either initial, intermediate or final -- in the synthesis of known or new pharmaceuticals, e.g., antivirals, antibiotics, and analgesics.

Combinatorial Libraries

The subject methods of the present invention readily lend themselves to the creation of combinatorial libraries of compounds for the screening of pharmaceutical, agrochemical or other biological or medical activity or material-related qualities. A combinatorial library for the purposes of the present invention is a mixture of chemically related compounds which may be screened together for a desired property; said libraries may be in solution or

covalently linked to a solid support. The preparation of many related compounds in a single reaction greatly reduces and simplifies the number of screening processes which need to be carried out. Screening for the appropriate biological, pharmaceutical, agrochemical or physical property may be done by conventional methods.

5 Diversity in a library can be created at a variety of different levels. For instance, the substrate aryl groups used in a combinatorial approach can be diverse in terms of the core aryl moiety, e.g., a variegation in terms of the ring structure, and/or can be varied with respect to the other substituents.

A variety of techniques are available in the art for generating combinatorial libraries
10 of small organic molecules. See, for example, Blondelle et al. (1995) Trends Anal. Chem. 14:83; the Affymax U.S. Patents 5,359,115 and 5,362,899; the Ellman U.S. Patent 5,288,514; the Still et al. PCT publication WO 94/08051; Chen et al. (1994) JACS 116:2661; Kerr et al. (1993) JACS 115:252; PCT publications WO92/10092, WO93/09668 and WO91/07087; and the Lerner et al. PCT publication WO93/20242). Accordingly, a
15 variety of libraries on the order of about 16 to 1,000,000 or more diversomers can be synthesized and screened for a particular activity or property.

In an exemplary embodiment, a library of substituted diversomers can be synthesized using the subject reactions adapted to the techniques described in the Still et al. PCT publication WO 94/08051, e.g., being linked to a polymer bead by a hydrolyzable or
20 photolabile group, e.g., located at one of the positions of substrate. According to the Still et al. technique, the library is synthesized on a set of beads, each bead including a set of tags identifying the particular diversomer on that bead. In one embodiment, which is particularly suitable for discovering enzyme inhibitors, the beads can be dispersed on the surface of a permeable membrane, and the diversomers released from the beads by lysis of
25 the bead linker. The diversomer from each bead will diffuse across the membrane to an assay zone, where it will interact with an enzyme assay.

Exemplification

The invention now being generally described, it will be more readily understood by reference to the following examples which are included merely for purposes of illustration
30 of certain aspects and embodiments of the present invention, and are not intended to limit the invention.

Example 1General Procedure A -- Arylations Using Aryl or Heteroaryl Iodides

An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 1.0 mol%), amide (1.2 mmol) and K₃PO₄ (2.1 mmol), evacuated and backfilled with argon.

5 *trans*-1,2-Cyclohexanediamine (13 µL, 0.108 mmol, 11 mol%), dodecane (235 µL), aryl iodide (1.0 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was

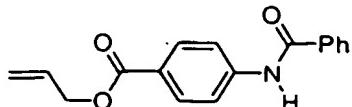
10 purified by flash chromatography to afford pure product.

Example 2General Procedure B -- Arylations Using Aryl or Heteroaryl Iodides

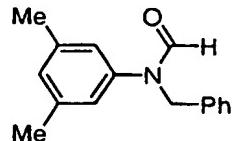
To a flame-dried resealable Schlenk tube was added CuI (2.0 mg, 0.0105 mmol, 1.0 mol%), the heterocycle (1.2 mmol) and K₃PO₄ (2.1 mmol), evacuated twice and back-filled with argon. Dodecane (45 µL, 0.20 mmol), 5-iodo-*m*-xylene (144 µL, 1.0 mmol), *trans*-1,2-cyclohexanediamine (12 µL, 0.10 mmol, 10 mol%) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction was stirred with heating via an oil bath at 110 °C for 20 hours. The reaction mixture was cooled to ambient temperature, diluted with 2-3 mL ethyl acetate, and filtered through a plug of silica gel eluting with 10-20 mL of ethyl acetate. The filtrate was concentrated and the resulting residue was purified by column chromatography to provide the purified product.

Example 3General Procedure C – Arylations Using Aryl or Heteroaryl Bromides

An oven-dried resealable Schlenk tube containing a stirbar was charged with CuI (20 mg, 0.1 mmol, 10 mol%), amide (1.2 mmol) and K₃PO₄ (425 mg, 2 mmol), evacuated and backfilled with argon. *trans*-1,2-Diaminocyclohexane (11.5 mg, 0.1 mmol), heteroaryl bromide (1.0 mmol) and dioxane (1 ml) were injected, and under a flow of argon, the septum was replaced by a Teflon screw cap. The tube was sealed, and the mixture was stirred and heated in an oil bath at 110 °C for the time specified. The resulting mixture was cooled to room temperature and filtered through Celite with dichloromethane. The filtrate was concentrated under reduced pressure and the residue chromatographed on silica gel.

Example 4**N-(4-Allyloxycarbonylphenyl)benzamide**

Using general procedure A, benzamide (150 mg, 1.24 mmol) was coupled with allyl 5 4-iodobenzoate (300 mg, 1.04 mmol). The crude product was purified by flash chromatography on silica gel (2x15 cm; hexane-ethyl acetate 3:1; 10 mL fractions). Fractions 8-15 provided 266 mg (91% yield) of the product as white crystals. ¹H NMR (400 MHz, CDCl₃): δ 8.14-8.09 (m, 2H), 8.00 (br s, 1H), 7.93-7.88 (m, 2H), 7.80-7.75 (m, 2H), 7.63-7.58 (m, 1H), 7.56-7.51 (m, 2H), 6.07 (ddt, J = 17.2, 11.7, 5.6 Hz, 1H), 5.45 (dq, J = 10 17.2, 1.4 Hz, 1H), 5.32 (dq, J = 11.7, 1.4 Hz, 1H), 4.85 (dt, J = 5.6, 1.4 Hz, 2H).

Example 5**N-Benzyl-N-(3,5-dimethylphenyl)formamide**

Using general procedure A, N-benzylformamide (170 mg, 1.26 mmol) was coupled 15 with 5-iodo-m-xylene (150 μL, 1.04 mmol). The crude product was purified by flash chromatography on silica gel (2x15 cm; hexane-ethyl acetate 3:1; 15 mL fractions). Fractions 7-13 provided 247 mg (99% yield) of the product as a colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 8.55 (s, 1H), 7.39-7.22 (m, 5H), 6.91 (s, 1H), 6.75 (s, 2H), 5.00 (s, 2H), 2.30 (s, 6H).

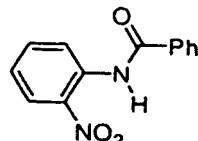
Example 6**N-(2-Dimethylaminophenyl)benzamide**

Using general procedure A, benzamide (150 mg, 1.24 mmol) was coupled with 25 N,N-dimethyl-2-iodoaniline (160 μL, 1.05 mmol). The crude product was purified by flash chromatography on silica gel (2x15 cm; hexane-ethyl acetate 7:1; 15 mL fractions).

Fractions 8-15 provided 239 mg (95% yield) of the product as a pale yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 9.42 (br s, 1H), 8.57 (dd, $J = 7.8, 1.4$ Hz, 1H), 7.98-7.92 (m, 2H), 7.62-7.51 (m, 3H), 7.26 (dd, $J = 7.8, 1.4$ Hz, 1H), 7.22 (td, $J = 7.8, 1.4$ Hz, 1H), 7.12 (td, $J = 7.8, 1.4$ Hz, 1H), 2.74 (s, 6H).

5 **Example 7**

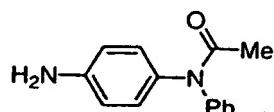
N-(2-Nitrophenyl)benzamide



Using general procedure A, benzamide (150 mg, 1.24 mmol) was coupled with 1-iodo-2-nitrobenzene (260 mg, 1.04 mmol). The crude product was purified by flash chromatography on silica gel (2x15 cm; hexane-ethyl acetate 8:1; 15 mL fractions). Fractions 8-14 provided 177 mg (70% yield) of the product as bright yellow needles. The ^1H NMR spectrum was in accord with that reported by Murphy et al. Murphy, J. A.; Rasheed, F.; Gastaldi, S.; Ravishanker, T.; Lewis, N. *J. Chem. Soc., Perkin Trans 1* 1997, 1549.

15 **Example 8**

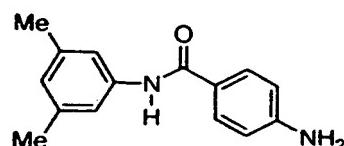
N-(4-Aminophenyl)-*N*-phenylacetamide



Using general procedure A, acetanilide (165 mg, 1.22 mmol) was coupled with 4-iodoaniline (228 mg, 1.04 mmol). The crude product was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate 1:4; 20 mL fractions). Fractions 10-20 provided 192 mg (82% yield) of the product as a pale yellow solid. ^1H NMR (400 MHz, CDCl_3): δ 7.50-7.10 (m, 5H), 7.09-7.04 (m, 2H), 6.74-6.61 (m, 2H), 3.90-3.50 (br s, 2H), 2.07 (s, 3H).

Example 9

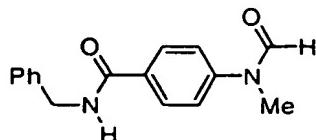
25 *4-Amino-*N*-(3,5-dimethylphenyl)benzamide*



Using general procedure A, 4-aminobenzamide (170 mg, 1.25 mmol) was coupled with 5-iodo-*m*-xylene (150 µL, 1.04 mmol). The crude product was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate 2:3; 15 mL fractions). Fractions 9-18 provided 246 mg (98% yield) of the product as a white solid. ¹H NMR (400 MHz, CDCl₃): δ 7.74-7.69 (m, 2H), 7.66 (br s, 1H), 7.28 (s, 2H), 6.78 (s, 1H), 6.74-6.69 (m, 2H), 4.05 (br s, 2H), 2.33 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 165.7, 150.3, 139.1, 138.6, 129.2, 126.2, 124.8, 118.2, 114.6, 21.8.

Example 10

N-(4-Benzylaminocarbonylphenyl)-N-methylformamide



10

An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 1.0 mol%), 4-iodo-*N*-benzylbenzamide (350 mg, 1.04 mmol), K₃PO₄ (450 mg, 2.12 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (13 µL, 0.108 mmol, 11 mol%), dodecane (235 µL), *N*-methylformamide (74 µL, 1.27 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x15 cm; ethyl acetate-dichloromethane 2:1; 20 mL fractions). Fractions 7-18 provided 273 mg (98% yield) of the product as white crystals. ¹H NMR (400 MHz, CDCl₃): δ 8.57 (s, 1H), 7.90-7.86 (m, 2H), 7.40-7.29 (m, 5H), 7.25-7.20 (m, 2H), 6.62 (br s, 1H), 4.66 (d, *J* = 5.7 Hz, 2H), 3.35 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 166.6, 162.3, 145.2, 138.4, 132.2, 129.2, 129.0, 128.3, 128.1, 121.5, 44.6, 32.0.

15

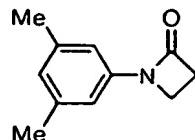
The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x15 cm; ethyl acetate-dichloromethane 2:1; 20 mL fractions). Fractions 7-18 provided 273 mg (98% yield) of the product as white crystals. ¹H NMR (400 MHz, CDCl₃): δ 8.57 (s, 1H), 7.90-7.86 (m, 2H), 7.40-7.29 (m, 5H), 7.25-7.20 (m, 2H), 6.62 (br s, 1H), 4.66 (d, *J* = 5.7 Hz, 2H), 3.35 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 166.6, 162.3, 145.2, 138.4, 132.2, 129.2, 129.0, 128.3, 128.1, 121.5, 44.6, 32.0.

20

The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x15 cm; ethyl acetate-dichloromethane 2:1; 20 mL fractions). Fractions 7-18 provided 273 mg (98% yield) of the product as white crystals. ¹H NMR (400 MHz, CDCl₃): δ 8.57 (s, 1H), 7.90-7.86 (m, 2H), 7.40-7.29 (m, 5H), 7.25-7.20 (m, 2H), 6.62 (br s, 1H), 4.66 (d, *J* = 5.7 Hz, 2H), 3.35 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 166.6, 162.3, 145.2, 138.4, 132.2, 129.2, 129.0, 128.3, 128.1, 121.5, 44.6, 32.0.

25

N-(3,5-Dimethylphenyl)-2-azetidinone

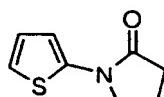


Using general procedure A, 2-azetidinone (88 mg, 1.24 mmol) was coupled with 5-iodo-*m*-xylene (150 μ L, 1.04 mmol). The crude product was purified by flash chromatography on silica gel (2x15 cm; hexane-ethyl acetate 1:1; 15 mL fractions).

Fractions 5-10 provided 173 mg (95% yield) of the product as a white solid. 1 H NMR (400 MHz, CDCl₃): δ 7.01 (s, 2H), 6.76 (s, 1H), 3.61 (t, J = 4.5 Hz, 2H), 3.10 (t, J = 4.5 Hz, 2H), 2.32 (s, 6H).

Example 12

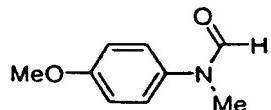
N-(2-Thiophenyl)-2-pyrrolidinone



An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 1.0 mol%) and K₃PO₄ (450 mg, 2.12 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (13 μ L, 0.108 mmol, 11 mol%), dodecane (235 μ L), 2-iodothiophene (115 μ L, 1.04 mmol), 2-pyrrolidinone (94 μ L, 1.24 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x15 cm; hexane-ethyl acetate 1:1; 20 mL fractions). Fractions 9-15 provided 174 mg (100% yield) of the product as white crystals. 1 H NMR (400 MHz, CDCl₃): δ 6.95 (dd, J = 5.5, 1.3 Hz, 1H), 6.90 (dd, J = 5.5, 3.7 Hz, 1H), 6.55 (dd, J = 3.7, 1.3 Hz, 1H), 3.92 (t, J = 7.4 Hz, 2H), 2.66 (t, J = 7.4 Hz, 2H), 2.27 (p, J = 7.4 Hz, 2H). 13 C NMR (100 MHz, CDCl₃): δ 172.4, 140.9, 124.2, 118.4, 110.9, 49.2, 31.7, 18.3.

Example 13

Preparation of N-(4-methoxyphenyl)-N-methylformamide using 0.2 mol% CuI

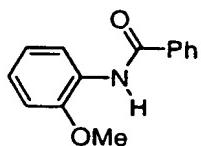


An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 0.2 mol%) and K₃PO₄ (2.25 g, 10.6 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (33 μ L, 0.269 mmol, 5.2 mol%), dodecane (1.20 mL), 4-iodoanisole

(1.22 g, 5.21 mmol), *N*-methylformamide (360 μ L, 6.15 mmol) and dioxane (5.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting suspension was cooled to room temperature and filtered through a 1.5x10 cm pad of silica gel eluting with 50 mL of ethyl acetate. The light green filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x15 cm; hexane-ethyl acetate 1:1; 20 mL fractions). Fractions 8-17 provided 840 mg (98% yield) of the product as a colorless oil. The 1 H NMR spectrum was in accord with that reported by Hoffman et al. Hoffman, R. V.; Salvador, J. M. *J. Org. Chem.* 1992, 57, 4487.

10 *Example 14*

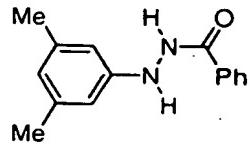
Preparation of *N*-(2-methoxyphenyl)benzamide at 40 °C



Using general procedure A, benzamide (150 mg, 1.24 mmol) was coupled with 2-iodoanisole (135 μ L, 1.04 mmol) at 40 °C for 18 h. The crude product was purified by flash chromatography on silica gel (2x15 cm; hexane-ethyl acetate 3:1; 15 mL fractions). Fractions 8-12 provided 49 mg (21% yield) of the product as a colorless oil. The 1 H NMR spectrum was in accord with that reported by Narasaka et al. Tsutsui, H.; Ichikawa, T.; Narasaka, K. *Bull. Chem. Soc. Jpn.* 1999, 72, 1869.

Example 15

20 1-Benzoyl-2-(3,5-dimethylphenyl)hydrazine

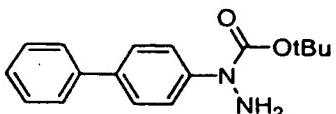


An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 1.0 mol%), benzoic hydrazide (170 mg, 1.25 mmol), K₂CO₃ (290 mg, 2.10 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (13 μ L, 0.108 mmol, 11 mol%), dodecane (235 μ L), 5-iodo-*m*-xylene (150 μ L, 1.04 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting suspension was cooled to room temperature

and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x15 cm; hexane-ethyl acetate 2:1; 15 mL fractions). Fractions 9-13 provided 159 mg (64% yield) of the product as a pale tan solid. ^1H NMR (300 MHz, CDCl_3): δ 8.06 (br s, 5 1H), 7.87-7.82 (m, 2H), 7.60-7.44 (m, 3H), 6.58 (s, 1H), 6.54 (s, 2H), 6.32 (br s, 1H), 2.25 (s, 6H).

Example 16

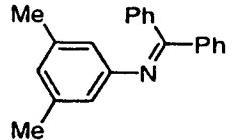
1-*tert*-Butoxycarbonyl-1-(4-phenylphenyl)hydrazine



An oven-dried resealable Schlenk tube was charged with CuI (50 mg, 0.263 mmol, 5.1 mol%), 1,10-phenanthroline (100 mg, 0.555 mmol, 11 mol%), 4-iodobiphenyl (1.45 g, 5.18 mmol), Cs₂CO₃ (2.30 g, 7.06 mmol), evacuated and backfilled with argon. *tert*-Butyl carbazate (825 mg, 6.24 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting suspension was cooled to room temperature and filtered through a 1x1 cm pad of silica gel eluting with 50 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate 4:1; 20 mL fractions). Fractions 9-20 provided 1.29 g (88% yield) of the product as a light yellow solid. ¹H NMR (400 MHz, CDCl₃): δ 7.64-7.59 (m, 2H), 7.57 (s, 4H), 7.48-7.43 (m, 2H), 7.38-7.33 (m, 1H), 4.50 (s, 2H), 1.56 (s, 9H).

Example 17

N-(3,5-Dimethylphenyl) benzophenone imine



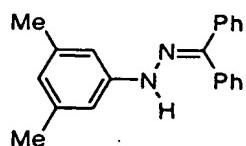
An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol,
 25 1.0 mol%), sodium *tert*-butoxide (150 mg, 1.56 mmol), evacuated and backfilled with
 argon. *trans*-1,2-Cyclohexanediamine (13 µL, 0.108 mmol, 11 mol%), dodecane (235 µL),
 5-iodo-*m*-xylene (150 µL, 1.04 mmol), benzophenone imine (210 µL, 1.25 mmol) and
 dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction

mixture was stirred magnetically at 110 °C for 36 h. The resulting dark brown suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x15 cm; hexane-ethyl acetate 30:1; 15 mL fractions).

5 Fractions 6-11 provided 46 mg (15% yield) of the product as a pale tan solid. ¹H NMR (300 MHz, CDCl₃): δ 7.79-7.75 (m, 2H), 7.52-7.40 (m, 3H), 7.34-7.26 (m, 3H), 7.20-7.15 (m, 2H), 6.60 (s, 1H), 6.39 (s, 2H) 2.19 (s, 6H).

Example 18

N-(3,5-Dimethylphenyl) benzophenone hydrazone

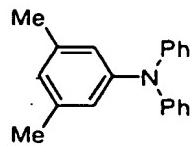


10

An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 1.0 mol%), benzophenone hydrazone (245 mg, 1.25 mmol), sodium *tert*-butoxide (145 mg, 1.51 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (13 μL, 0.108 mmol, 11 mol%), dodecane (235 μL), 5-iodo-*m*-xylene (150 μL, 1.04 mmol) and 15 dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting dark brown suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of hexane-ethyl acetate 5:1. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate 40:1; 15 mL fractions). Fractions 10-12 provided 251 mg (80% yield) of the product as a bright yellow solid. The ¹H NMR spectrum was in accord with that reported by Buchwald et al. Wagaw, S.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* 1999, 44, 10251.

Example 19

N-(3,5-Dimethylphenyl)-N,N-diphenylamine



25

An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 1.0 mol%), diphenylamine (210 mg, 1.24 mmol), sodium *tert*-butoxide (145 mg, 1.51

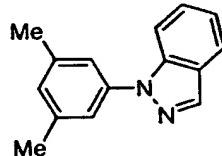
mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (13 μ L, 0.108 mmol, 11 mol%), dodecane (235 μ L), 5-iodo-*m*-xylene (150 μ L, 1.04 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 24 h. The resulting pale brown suspension was

5 cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of hexane-ethyl acetate 5:1. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x25 cm; hexane-ethyl acetate 40:1; 15 mL fractions). Fractions 9-13 provided 211 mg (74% yield) of the product as white crystals.

The 1 H NMR spectrum was in accord with that reported by Goodbrand et al. Goodbrand,
10 H. B.; Hu, N. X. *J. Org. Chem.* 1999, 64, 670.

Example 20

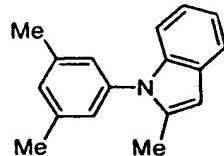
1-(3,5-Dimethylphenyl)indazole



Using general procedure A, indazole (148 mg, 1.25 mmol) was coupled with 5-iodo-*m*-xylene (150 μ L, 1.04 mmol). The crude product was purified by flash chromatography on
15 silica gel (2x15 cm; hexane-ethyl acetate 10:1; 10 mL fractions). Fractions 4-10 provided 222 mg (96% yield) of the product as a pale yellow oil. 1 H NMR (300 MHz, CDCl₃): δ 8.20 (d, *J* = 1.0 Hz, 1H), 7.83-7.74 (m, 2H), 7.46-7.40 (m, 1H), 7.36 (s, 2H), 7.25-7.19 (m, 1H), 7.01 (s, 1H), 2.43 (s, 6H).

20 **Example 21**

N-(3,5-Dimethylphenyl)-2-methylindole



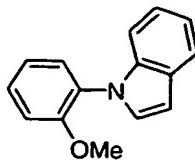
Using general procedure A, 2-methylindole (165 mg, 1.26 mmol) was coupled with 5-iodo-*m*-xylene (150 μ L, 1.04 mmol). The crude product was purified by flash
25 chromatography on silica gel (2x15 cm; hexane-ether 40:1; 15 mL fractions). Fractions 4-9 provided 232 mg (95% yield) of the product as a colorless oil. 1 H NMR (300 MHz, CDCl₃):

δ 7.62-7.53 (m, 1H), 7.15-7.05 (m, 4H), 6.98 (s, 2H), 6.39 (s, 1H), 2.41 (s, 6H), 2.31 (d, J = 1.0 Hz, 3H).

Example 22

N-(2-Methoxyphenyl)indole

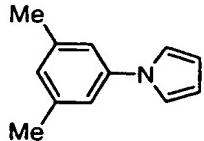
5



Using general procedure A, indole (146 mg, 1.25 mmol) was coupled with 2-iodoanisole (135 μ L, 1.04 mmol). The crude product was purified by flash chromatography on silica gel (2x15 cm; hexane-ether 15:1; 15 mL fractions). Fractions 6-10 provided 232 mg (100% yield) of the product as a colorless oil. The 1 H NMR spectrum was in accord with that reported by Maiorana et al. Maiorana, S.; Baldoli, C.; Del Buttero, P.; Di Ciolo, M.; Papagni, A. *Synthesis* 1998, 735.

Example 23

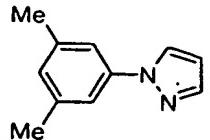
1-(3,5-Dimethylphenyl)pyrrole



15 Using general procedure B, pyrrole (83 μ L, 1.2 mmol) was coupled with 5-iodo-*m*-xylene to give the crude product. Column chromatography (2x15 cm, hexane:ethyl acetate 9:1) provided 0.170 g (99% yield) of the product as a colorless oil. 1 H NMR (400 MHz, CDCl₃): δ 7.07 (t, J = 7.0 Hz, 2H), 7.02 (s, 2H), 6.89 (s, 1H), 6.33 (t, J = 7.0 Hz, 2H), 2.37 (s, 6H).

20 **Example 24**

1-(3,5-Dimethylphenyl)-1-pyrazole

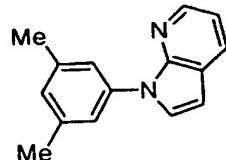


Using general procedure B, pyrazole (0.082 g, 1.2 mmol) was coupled with 5-iodo-*m*-xylene using K₂CO₃ (2.1 mmol) as the base to give the crude product. Column chromatography (2x15 cm, hexane:ethyl acetate 9:1) provided 0.153 g (89% yield) of the

product as a colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 7.90 (d, $J = 2.2$ Hz, 1H), 7.71 (d, $J = 1.5$ Hz, 1H), 7.32 (s, 2H), 6.93 (s, 1H), 6.44 (t, $J = 2.2$ Hz, 1H), 2.38 (s, 6H).

Example 25

1-(3,5-Dimethylphenyl)-1-(7-azaindole)



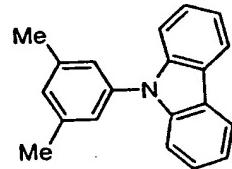
5

Using general procedure B, 7-azaindole (0.142 g, 1.2 mmol) was coupled with 5-iodo-*m*-xylene to give the crude product. Column chromatography (2x15 cm, hexane:ethyl acetate 5:1) provided 0.220 g (99% yield) of the product as a white solid. ^1H NMR (400 MHz, CDCl_3): δ 8.38 (dd, $J = 1.5$ Hz and $J = 4.7$ Hz, 1H), 7.97 (dd, $J = 1.5$ Hz and $J = 7.8$ Hz, 1H), 7.48 (d, $J = 3.6$ Hz, 1H), 7.33 (s, 2H), 7.12 (dd, $J = 4.7$ Hz and $J = 7.8$ Hz, 1H), 6.99 (s, 1H), 6.60 (d, $J = 3.6$ Hz, 1H), 2.41 (s, 6H).

10

Example 26

1-(3,5-Dimethylphenyl)carbazole



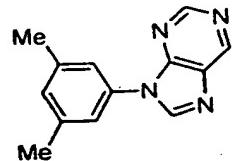
15

Using general procedure B, pyrrole (83 μL , 1.2 mmol) was coupled with 5-iodo-*m*-xylene to give the crude product. Column chromatography (2x15 cm, hexane:ethyl acetate 50:1) provided 0.268 g (99% yield) of the product as a white solid. ^1H NMR (400 MHz, CDCl_3): δ 8.15 (d, $J = 7.8$ Hz, 2H), 7.41 (m, 4H), 7.28 (m, 2H), 7.18 (s, 2H), 7.11 (s, 1H), 2.43 (s, 6H).

20

Example 27

1-(3,5-Dimethylphenyl)-1-purine

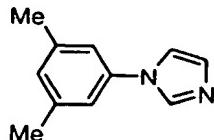


Using general procedure B, purine (0.144 g, 1.2 mmol) was coupled with 5-iodo-*m*-xylene using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), Cs_2CO_3 (2.1 mmol), *trans*-1,2-

cyclohexanediamine (24 μ L, 0.20 mmol, 20 mol%) and dimethylformamide (1.0 mL) to give the crude product. Column chromatography (2x15 cm, hexane:ethyl acetate 1:1) provided 0.073 g (33% yield) of the product as a white solid. 1 H NMR (400 MHz, CDCl₃): δ 9.24 (s, 1H), 9.06 (s, 1H), 8.34 (s, 1H), 7.31 (s, 2H), 7.13 (s, 1H), 2.44 (s, 6H).

5 **Example 28**

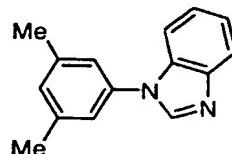
1-(3,5-Dimethylphenyl)-1-imidazole



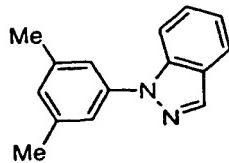
Using general procedure B, imidazole (0.102 g, 1.2 mmol) was coupled with 5-iodo-*m*-xylene using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), Cs₂CO₃ (2.1 mmol), *trans*-1,2-cyclohexanediamine (24 μ L, 0.20 mmol, 20 mol%) and dioxane (1.0 mL) to give the crude product. Column chromatography (2x15 cm, hexane:ethyl acetate 1:4) provided 0.142 g (82% yield) of the product as a clear viscous oil. 1 H NMR (400 MHz, CDCl₃): δ 7.84 (s, 1H), 7.25 (d, J = 1Hz, 1H), 7.19 (d, J = 1Hz, 1H), 7.00 (s, 3H), 2.37 (s, 6H).

Example 29

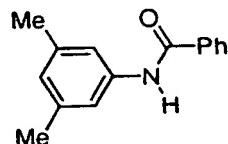
15 **1-(3,5-Dimethylphenyl)-1-benzimidazole**



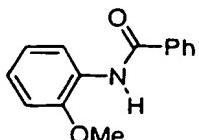
Using general procedure B, benzimidazole (0.144 g, 1.2 mmol) was coupled with 5-iodo-*m*-xylene using CuI (0.019 g, 0.10 mmol, 10 mol%), Cs₂CO₃ (2.1 mmol), 1,10-phenanthroline (0.036 g, 0.20 mmol, 20 mol%) and dimethylformamide (0.5 mL) to give the crude product. Column chromatography (2x15 cm, hexane:ethyl acetate 1:1) provided 0.205 g (92% yield) of the product as a white solid. 1 H NMR (400 MHz, CDCl₃): δ 8.10 (s, 1H), 7.87 (m, 1H), 7.55 (m, 1H), 7.33 (m, 2H), 7.13 (s, 2H), 7.10 (s, 1H), 2.43 (s, 6H).

Example 301-(3,5-Dimethylphenyl)-1-indazole

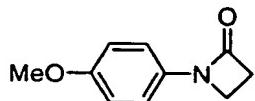
Using general procedure B, indazole (0.142 g, 1.2 mmol) was coupled with 5-iodo-
5 *m*-xylene however the reaction was run at room temperature. Gas chromatographic analysis
of the crude reaction mixture after filtration as per the general procedure it was determined
that 52 % of the 5-iodo-*m*-xylene was consumed. The ratio of the title compound to 1-(3,5-
dimethylphenyl)-2-indazole was determined to be greater than 25 to 1 by GC analysis.

Example 3110 N-(3,5-Dimethylphenyl)benzamide

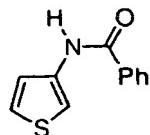
An oven-dried resealable Schlenk tube was charged with CuI (4.0 mg, 0.0210 mmol,
1.0 mol%), benzamide (300 mg, 2.48 mmol), K₂CO₃ (600 mg, 4.38 mmol), evacuated and
backfilled with argon. *trans*-1,2-Cyclohexanediamine (26 µL, 0.216 mmol, 11 mol%), 5-
15 bromo-*m*-xylene (280 µL, 2.06 mmol) and dioxane (1.0 mL) were added under argon. The
Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23
h. The resulting suspension was cooled to room temperature and filtered through a 0.5x1 cm
pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the
residue was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate
20 3:1; 15 mL fractions). Fractions 10-15 provided 419 mg (90% yield) of the product as
white crystals. ¹H NMR (400 MHz, CDCl₃): δ 7.92-7.85 (m, 3H), 7.59-7.75 (m, 3H), 7.31
(s, 2H), 6.82 (s, 1H), 2.34 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 165.6, 138.7, 137.7,
135.1, 131.7, 128.7, 126.9, 126.3, 117.9, 21.3. IR (neat, cm⁻¹): 3300, 1649, 1614, 1547.

Example 32N-(2-Methoxyphenyl)benzamide

An oven-dried resealable Schlenk tube was charged with CuI (6.0 mg, 0.0315 mmol, 5 1.0 mol%), benzamide (460 mg, 3.80 mmol), K₂CO₃ (850 mg, 6.15 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (40 µL, 0.333 mmol, 11 mol%), 2-bromoanisole (0.38 mL, 3.05 mmol) and dioxane (0.50 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting suspension was cooled to room temperature and filtered through a 0.5x1 cm 10 pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate 5:1; 20 mL fractions). Fractions 10-15 provided 573 mg (83% yield) of the product as a colorless oil. The ¹H NMR spectrum was in accord with that reported by Narasaka et al. Tsutsui, H.; Ichikawa, T.; Narasaka, K. *Bull. Chem. Soc. Jpn.* 1999, 72, 1869.

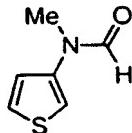
Example 33N-(4-Methoxyphenyl)-2-azetidinone

An oven-dried resealable Schlenk tube was charged with CuI (6.0 mg, 0.0315 mmol, 1.0 mol%), 2-azetidinone (300 mg, 4.22 mmol), K₂CO₃ (850 mg, 6.15 mmol), evacuated 20 and backfilled with argon. *trans*-1,2-Cyclohexanediamine (40 µL, 0.333 mmol, 11 mol%), 4-bromoanisole (0.38 mL, 3.04 mmol) and dioxane (0.50 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the 25 residue was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate 1:1; 20 mL fractions). Fractions 10-22 provided 320 mg (59% yield) of the product as white crystals. ¹H NMR (400 MHz, CDCl₃): δ 7.35-7.29 (m, 2H), 6.91-6.86 (m, 2H), 3.81 (s, 3H), 3.60 (t, J = 4.4 Hz, 2H), 3.11 (t, J = 4.4 Hz, 2H).

Example 34**N-Thiophen-3-yl-benzamide**

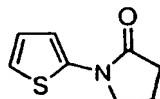
Using general procedure C, 3-bromothiophene was coupled with benzamide with the reaction time of 21 h. Chromatography gave 198.9 mg (98%) of the title compound as a solid. ^1H NMR (CDCl_3 , 300 MHz): δ 8.34 (br s, 1H), 7.85 (dd, 2H, J = 1.2, 8.1 Hz), 7.72 (dd, 1H, J = 1.2, 3.0 Hz), 7.55-7.41 (m, 3H), 7.26 (dd, 1H, J = 3.3, 4.8 Hz), 7.14 (dd, 1H, J = 1.5, 5.4 Hz).

Example 35
10 N-Methyl-N-thiophen-3-yl-formamide

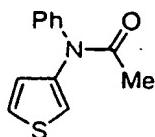


Using general procedure C with the exception that CuI (10 mg, 0.05 mmol, 5 mol%) was used, 3-bromothiophene was coupled with *N*-methylformamide with the reaction time of 24 h. Chromatography gave 114 mg (81%) of the title compound as an oil. ^1H NMR (CDCl_3 , 300 MHz): δ 8.36 (s, 0.8H), 7.71 (s, 0.2H), 7.49 (dd, 0.2H, J = 1.5, 5.4 Hz), 7.08 (dd, 0.2H, J = 1.2, 3.0 Hz), 6.80 (dd, 0.2H, J = 3.3, 5.4 Hz), 6.64 (dd, 0.8H, J = 3.3, 5.1 Hz), 6.30 (dd, 0.8H, J = 1.8, 5.4 Hz), 5.98 (dd, 0.8H, J = 1.2, 3.0 Hz), 2.79 (s, 2.4H), 2.21 (s, 0.6H).

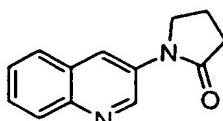
Example 36
20 1-Thiophen-2-yl-pyrrolidin-2-one



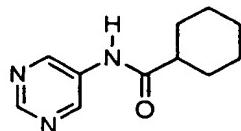
Using general procedure C, 2-bromothiophene was coupled with 2-pyrrolidinone with the reaction time of 16 h. Chromatography gave 158 mg (95%) of the title compound as a solid. ^1H NMR (CDCl_3 , 300 MHz): δ 6.94-6.86 (m, 2H), 6.53 (br s, 1H), 3.89 (t, 2H, J = 7.2 Hz), 2.63 (t, 2H, J = 8.1 Hz), 2.24 (p, 2H, J = 7.5 Hz).

Example 37**N-Phenyl-N-thiophen-3-yl-acetamide**

Using general procedure C, 3-bromothiophene was coupled with acetanilide with the
 5 reaction time of 15 h. Chromatography gave 178 mg (82%) of the title compound as an oil.
¹H NMR (CDCl₃, 300 MHz): δ 7.44 (br s, 3H), 7.28 (s, 2H), 7.18 (s, 2H), 6.94 (d, 1H, J = 4.8 Hz), 1.99 (br s, 3H).

Example 38**1-Quinolin-3-yl-pyrrolidin-2-one**

10 Using general procedure C, 3-bromoquinoline was coupled with 2-pyrrolidinone with the reaction time of 15 h. Chromatography gave 210 mg (99%) of the title compound as a solid. ¹H NMR (CDCl₃, 300 MHz): δ 9.24 (d, 1H, J = 2.7 Hz), 8.45 (d, 1H, J = 2.4 Hz), 8.08 (d, 1H, J = 8.4 Hz), 7.82 (d, 1H, J = 8.1 Hz), 7.66 (t, 1H, J = 7.7 Hz), 7.55 (t, 1H, J = 7.5 Hz), 4.04 (t, 2H, J = 7.2 Hz), 2.69 (t, 2H, J = 8.1 Hz), 2.28 (p, 2H, J = 7.8 Hz).

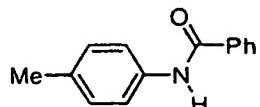
Example 39**Cyclohexanecarboxylic acid pyrimidin-5-yl-amide**

An oven-dried resealable Schlenk tube containing a stirbar was charged with CuI
 20 (20 mg, 0.1 mmol, 10 mol%), cyclohexanecarboxamide (153 mg, 1.2 mmol), 5-
bromopyrimidine (160 mg, 1 mmol), and K₃PO₄ (425 mg, 2 mmol), evacuated and
 backfilled with argon. *N,N'*-Dimethylethylenediamine (8.9 mg, 0.1 mmol) and dioxane (1
 ml) were injected, and under a flow of argon, the septum was replaced by a Teflon screw
 cap. The tube was sealed, and the mixture was stirred and heated in an oil bath at 110 °C for
 25 16 h. The contents of the tube were then partitioned between water and dichloromethane.
 The aqueous layer was separated, and extracted two times with additional dichloromethane.

The organics were then combined, dried over Na_2SO_4 , filtered, concentrated under reduced pressure. The residue was chromatographed on silica gel followed by recrystallization from dichloromethane / hexane to give 154 mg (75%) of the title compound as a solid. ^1H NMR (CDCl_3 , 300 MHz): δ 9.02 (s, 2H), 8.97 (s, 1H), 7.40 (br s, 1H), 2.32 (tt, 1H, J = 3.6, 11.4 Hz), 2.10-1.20 (m, 10H).

Example 40

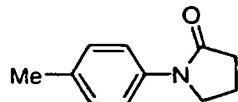
N-(4-Methylphenyl)benzamide



An oven-dried resealable Schlenk tube was charged with CuI (20 mg, 0.105 mmol, 10 5.1 mol%), benzamide (250 mg, 2.06 mmol), K_2CO_3 (600 mg, 4.34 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (26 μL , 0.217 mmol, 10.5 mol%) and 4-chlorotoluene (1.0 mL, 8.44 mmol) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 140 °C for 46 h. The resulting black suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate 2:1; 15 mL fractions). Fractions 5-15 were concentrated, the solid residue was suspended in 10 mL of hexane and filtered to provide 413 mg (95% yield) of the product as white crystals. The ^1H NMR spectrum was in accord with that reported by Erdik et al. Erdik, E.; Daskapan, T. *J. Chem. Soc., Perkin Trans. I* 1999, 3139.

Example 41

N-(4-Methylphenyl)-2-pyrrolidinone



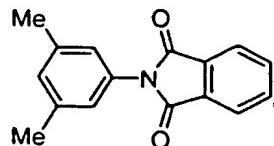
An oven-dried resealable Schlenk tube was charged with CuI (20 mg, 0.105 mmol, 25 5.1 mol%), K_2CO_3 (600 mg, 4.34 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (26 μL , 0.217 mmol, 11 mol%), 2-pyrrolidinone (155 μL , 2.04 mmol) and 4-chlorotoluene (1.0 mL, 8.44 mmol) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 140 °C for 42 h. The resulting suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica

gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate 3:7; 20 mL fractions). Fractions 10-20 provided 223 mg (62% yield) of the product as white crystals.

The ¹H NMR spectrum was in accord with that reported by Boeyens et al. Billing, D. G.;
 5 Boeyens, J. C. A.; Denner, L.; Du Plooy, K. E.; Long, G. C.; Michael, J. P. *Acta Cryst. (B)*
1991, B47, 284.

Example 42

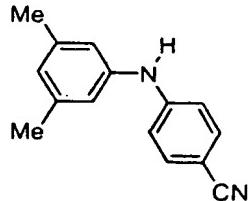
N-(3,5-Dimethylphenyl)phthalimide



An oven-dried resealable Schlenk tube was charged with CuI (200 mg, 1.05 mmol), phthalimide (185 mg, 1.26 mmol), K₂CO₃ (290 mg, 2.10 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (130 µL, 1.06 mmol), dodecane (235 µL), 5-iodo-*m*-xylene (150 µL, 1.04 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting brown suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x15 cm; hexane-ethyl acetate 3:1; 15 mL fractions). Fractions 8-11 provided 34 mg (13% yield) of the product as a tan solid. The ¹H NMR spectrum was in accord with that reported by Hashimoto et al.
 10
 15
 20 Shibata, Y.; Sasaki, K.; Hashimoto, Y.; Iwasaki, S. *Chem. Pharm. Bull.* **1996, 44**, 156.

Example 43

N-(3,5-Dimethylphenyl)-4-cyanoaniline

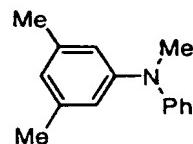


An oven-dried resealable Schlenk tube was charged with CuI (10 mg, 0.0525 mmol, 25 5.0 mol%), 1,10-phenanthroline (20 mg, 0.111 mmol), 4-cyanoaniline (146 mg, 1.24 mg), sodium *tert*-butoxide (145 mg, 1.51 mmol), evacuated and backfilled with argon. Dodecane

(235 μ L), 5-iodo-*m*-xylene (150 μ L, 1.04 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting brown suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The 5 filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x15 cm; hexane-ethyl acetate 5:1; 10 mL fractions). Fractions 7-16 provided 159 mg (69% yield) of the product as white crystals. 1 H NMR (400 MHz, CDCl₃): δ 7.51-7.47 (m, 2H), 6.91-6.95 (m, 2H), 6.83-6.80 (m, 2H), 6.80-6.78 (m, 1H), 6.02 (br s, 1H), 2.33 (q, *J*=0.5 Hz, 6H).

10 Example 44

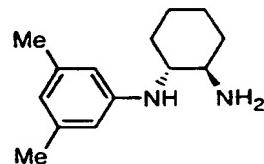
N-(3,5-Dimethylphenyl)-N-methylaniline



An oven-dried resealable Schlenk tube was charged with CuI (10 mg, 0.0525 mmol, 5.0 mol%), 1,10-phenanthroline (20 mg, 0.111 mmol), sodium *tert*-butoxide (145 mg, 1.51 mmol), evacuated and backfilled with argon. Dodecane (235 μ L), 5-iodo-*m*-xylene (150 μ L, 1.04 mmol), *N*-methylaniline (135 μ L, 1.25 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 24 h. The resulting brown suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The 15 filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x15 cm; hexane-ether 50:1; 10 mL fractions). Fractions 7-11 provided 110 mg (50% yield) of the product as a colorless oil. 1 H NMR (400 MHz, CDCl₃): δ 7.33-7.27 (m, 2H), 7.05-6.94 (m, 3H), 6.72 (s, 2H), 6.68 (s, 1H), 3.33 (s, 3H), 2.31 (s, 6H).

20 Example 45

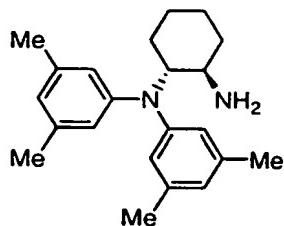
N-(3,5-Dimethylphenyl)-1,2-*trans*-cyclohexanediamine



An oven-dried resealable Schlenk tube was charged with CuI (40 mg, 0.210 mmol), K₂CO₃ (850 mg, 6.15 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (240 μL, 2.00 mmol) and 5-iodo-*m*-xylene (900 μL, 6.24 mmol) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred 5 magnetically at 100 °C for 23 h. The resulting purple-blue suspension was cooled to room temperature and filtered through a 2x1 cm pad of Celite eluting with 50 mL of dichloromethane. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; dichloromethane saturated with aq NH₃ - methanol 40:1; 15 mL fractions). Fractions 9-13 provided 178 mg (41% yield) of the product as a tan 10 solid. ¹H NMR (400 MHz, CDCl₃): δ 6.39 (s, 1H), 6.34 (s, 2H), 3.36 (br s, 1H), 3.03-2.92 (m, 1H), 2.56-2.46 (m, 1H), 2.25 (s, 6H), 2.20-2.10 (m, 1H), 2.08-1.95 (m, 1H), 1.83-1.70 (m, 2H), 1.55-1.20 (m, 5H), 1.10-1.00 (m, 1H).

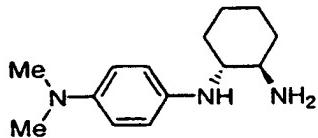
Example 46

N,N-bis-(3,5-Dimethylphenyl)-1,2-trans-cyclohexanediamine

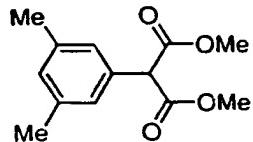


15

An oven-dried resealable Schlenk tube was charged with CuI (40 mg, 0.210 mmol), K₃PO₄ (1.30 g, 6.12 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (240 μL, 2.00 mmol), 5-iodo-*m*-xylene (900 μL, 6.24 mmol) and 2-methoxyethyl ether (1.0 mL) were added under argon. The Schlenk tube was sealed and the 20 reaction mixture was stirred magnetically at 140 °C for 24 h. The resulting dark brown suspension was cooled to room temperature and filtered through a 2x1 cm pad of Celite eluting with 50 mL of dichloromethane. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; chloroform - chloroform saturated with aq NH₃ - methanol 40:40:1; 15 mL fractions). Fractions 7-14 provided 465 mg (72% 25 yield) of the product as a tan solid. ¹H NMR (400 MHz, CDCl₃): δ 6.67 (s, 1H), 6.57 (s, 2H), 3.65-3.55 (m, 1H), 2.68-2.58 (m, 1H), 2.28 (s, 12H), 2.08-1.92 (m, 2H), 1.83-1.64 (m, 2H), 1.58-1.10 (m, 6H).

Example 47**N-(4-Dimethylaminophenyl)-1,2-trans-cyclohexanediamine**

An oven-dried resealable Schlenk tube was charged with CuI (190 mg, 0.998 mmol), K₃PO₄ (2.10 g, 9.89 mmol), 4-bromo-N,N-dimethylaniline (1.00 g, 5.00 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (0.60 L, 5.00 mmol) and dioxane (3.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 70 h. The resulting dark brown suspension was cooled to room temperature and filtered through a 2x1 cm pad of Celite eluting with 50 mL of dichloromethane. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; dichloromethane saturated with aq NH₃ - methanol 40:1; 20 mL fractions). Fractions 12-16 provided 692 mg (59% yield) of the product as a brown solid. ¹H NMR (400 MHz, CDCl₃): δ 6.75-6.63 (m, 4H), 3.00 (br s, 1H), 2.87-2.77 (m, 7H), 2.53-2.45 (m, 1H), 2.17-2.04 (m, 1H), 2.02-1.94 (m, 1H), 1.78-1.16 (m, 7H), 1.04-0.92 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 144.7, 140.9, 116.2, 116.1, 62.0, 56.5, 42.6, 35.7, 33.0, 25.8, 25.5.

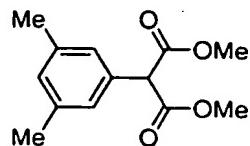
Example 48**Preparation of dimethyl 3,5-dimethylphenylmalonate using 1,10-phenanthroline as ligand for Cu**

An oven-dried resealable Schlenk tube was charged with CuI (10 mg, 0.0525 mmol, 5.0 mol%), 1,10-phenanthroline (20 mg, 0.111 mmol), Cs₂CO₃ (460 mg, 1.41 mmol), evacuated and backfilled with argon. Dodecane (235 μL), 5-iodo-*m*-xylene (150 μL, 1.04 mmol), dimethyl malonate (145 μL, 1.27 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting gray suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was

concentrated and the residue was purified by flash chromatography on silica gel (2x15 cm; hexane-ethyl acetate 6:1; 10 mL fractions). Fractions 9-15 provided 216 mg (88% yield) of the product as a colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 7.03 (s, 2H), 7.00 (s, 1H), 4.61 (s, 1H), 3.77 (s, 6H), 2.35 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 169.2, 138.7, 132.7, 130.5, 127.3, 57.8, 53.2, 21.7.

Example 49

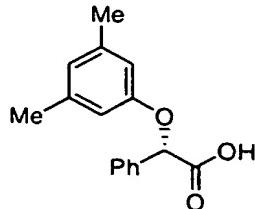
Preparation of dimethyl 3,5-dimethylphenylmalonate using *trans*-1,2-cyclohexanediamine as ligand for Cu



An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 1.0 mol%), K₃PO₄ (450 mg, 2.12 mmol), evacuated and backfilled with argon. Dodecane (235 μL), *trans*-1,2-cyclohexanediamine (13 μL, 0.108 mmol, 10 mol%), 5-iodo-*m*-xylene (150 μL, 1.04 mmol), dimethyl malonate (145 μL, 1.27 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting pale yellow suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate 5:1; 20 mL fractions). Fractions 10-16 provided 135 mg (55% yield) of the product as a colorless oil.

Example 50

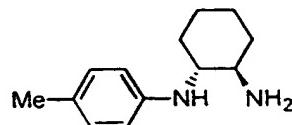
(S)-O-(3,5-Dimethylphenyl)mandelic acid



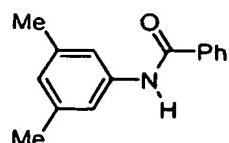
An oven-dried resealable Schlenk tube was charged with CuI (20 mg, 0.105 mmol, 10 mol%), (S)-mandelic acid (190 mg, 1.25 mmol), K₂CO₃ (430 mg, 3.11 mmol), evacuated and backfilled with argon. Dodecane (235 μL), 5-iodo-*m*-xylene (150 μL, 1.04 mmol), and *N,N*-dimethylacetamide (1.0 mL) were added under argon. The Schlenk tube

was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting pale yellow suspension was poured into 20 mL of 10% aq HCl and extracted with 3x20 mL of dichloromethane. The combined organic phase was dried (Na_2SO_4), concentrated, and the residue was purified by flash chromatography on silica gel (2x15 cm; hexane - ethyl acetate - acetic acid 40:20:1; 15 mL fractions). Fractions 7-13 provided 91 mg (34% yield) of the product as a white solid. ^1H NMR (400 MHz, CDCl_3): δ 10.65(br s, 1H), 7.64-7.57 (m, 2H), 7.47-7.36 (m, 3H), 6.67 (s, 1H), 6.61 (s, 2H), 5.65 (s, 1H), 2.28 (s, 6H).

Example 51
10 *N*-(4-Methylphenyl)-*trans*-1,2-cyclohexanediamine



An oven-dried resealable Schlenk tube was charged with CuI (190 mg, 0.998 mmol), K_3PO_4 (2.10 g, 9.89 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (0.60 mL, 5.00 mmol), 4-bromotoluene (0.70 mL, 5.69 mmol) and dioxane (3.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 70 h. The resulting dark brown suspension was cooled to room temperature and filtered through a 2x1 cm pad of Celite eluting with 50 mL of dichloromethane. The black filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; dichloromethane saturated with aq NH_3 - methanol 50:1; 15 mL fractions). Fractions 9-11 provided 650 mg (64% yield) of the product as a brown solid. ^1H NMR (400 MHz, CDCl_3): δ 7.00-6.95 (m, 2H), 6.62-6.57 (m, 2H), 3.30 (br s, 1H), 2.96-2.86 (br m, 1H), 2.49 (td, $J = 10.4, 3.6$, 1H), 2.23 (s, 3H), 2.17-2.08 (m, 1H), 2.02-1.94 (m, 1H), 1.79-1.66 (m, 2H), 1.44 (br s, 2H), 1.38-1.17 (m, 3H), 1.07-0.95 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 145.9, 129.7, 126.6, 113.9, 60.5, 56.1, 35.2, 32.4, 25.3, 25.0, 20.3.

Example 52**Preparation of N-(3,5-dimethylphenyl)benzamide at room temperature using N-(4-methylphenyl)-*trans*-1,2-cyclohexanediamine**

- 5 An oven-dried resealable Schlenk tube was charged with CuI (10 mg, 0.0525 mmol, 5.0 mol%), *trans*-N-(4-methylphenyl)-1,2-cyclohexanediamine (22 mg, 0.108 mmol, 10 mol%), benzamide (150 mg, 1.24 mmol), Cs₂CO₃ (650 mg, 1.99 mmol), evacuated and backfilled with argon. Dioxane (1.0 mL) and 5-iodo-*m*-xylene (150 µL, 1.04 mmol) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred
- 10 magnetically at room temperature for 46 h. The resulting suspension was filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate 3:1; 15 mL fractions). Fractions 8-15 provided 214 mg (91% yield) of the product as white crystals.

Example 53**Preparation of N-(3,5-dimethylphenyl)benzamide at 50 °C using N-(4-methylphenyl)-*trans*-1,2-cyclohexanediamine**

- An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 1.0 mol%), *N*-(4-methyl-phenyl)-*trans*-1,2-cyclohexanediamine (22 mg, 0.108 mmol, 10 mol%), benzamide (150 mg, 1.24 mmol), Cs₂CO₃ (650 mg, 1.99 mmol), evacuated and backfilled with argon. Dioxane (1.0 mL) and 5-iodo-*m*-xylene (150 µL, 1.04 mmol) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 50 °C for 23 h. The resulting light brown suspension was filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate 3:1; 15 mL fractions). Fractions 9-14 provided 228 mg (97% yield) of the product as a pale pink solid.

Example 54**Preparation of N-(3,5-dimethylphenyl)benzamide using 1,3-bis(2,4,6-trimethylphenyl)-imidazolium chloride**

A 10 mL pear-shape flask was charged with CuI (20 mg, 0.105 mmol, 5.0 mol%), 1,3-bis(2,4,6-trimethylphenyl)-imidazolium chloride (36 mg, 0.106 mmol, 5.1 mol%), evacuated and backfilled with argon. The flask was transferred into a glovebox, and NaOtBu (11 mg, 0.114 mmol, 5.5 mol%) was added under nitrogen. The flask was capped 5 with a septum and removed from the glovebox. Dioxane (2.0 mL) was added and the resulting light brown suspension was stirred at room temperature for 15 min. Meanwhile, an oven-dried resealable Schlenk tube was charged with benzamide (300 mg, 2.48 mmol), K₃PO₄ (900 mg, 4.24 mmol), evacuated and backfilled with argon. The Schlenk tube was capped with a rubber septum, and 5-iodo-*m*-xylene (300 μL, 2.08 mmol) was added under 10 argon. The catalyst suspension prepared above was transferred *via* a thick cannula to the reaction mixture in the Schlenk tube. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting brown suspension was cooled to room temperature, dodecane (470 μL, GC standard) was added, and the mixture was filtered through a Celite pad eluting with ethyl acetate. The GC 15 analysis of the filtrate indicated a 27% yield of the product.

Example 55

Preparation of *N*-(3,5-dimethylphenyl)benzamide using 1,3-bis(2,6-diisopropylphenyl)-imidazolinium chloride

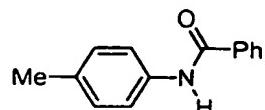
A 10 mL pear-shape flask was charged with CuI (20 mg, 0.105 mmol, 5.0 mol%), 20 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride (45 mg, 0.105 mmol, 5.0 mol%), evacuated and backfilled with argon. The flask was transferred into a glovebox, and NaOtBu (11 mg, 0.114 mmol, 5.5 mol%) was added under nitrogen. The flask was capped with a septum and removed from the glovebox. Dioxane (2.0 mL) was added and the resulting light brown suspension was stirred at room temperature for 15 min. Meanwhile, an 25 oven-dried resealable Schlenk tube was charged with benzamide (300 mg, 2.48 mmol), K₃PO₄ (900 mg, 4.24 mmol), evacuated and backfilled with argon. The Schlenk tube was capped with a rubber septum, and 5-iodo-*m*-xylene (300 μL, 2.08 mmol) was added under argon. The catalyst suspension prepared above was transferred *via* a thick cannula to the reaction mixture in the Schlenk tube. The Schlenk tube was sealed with a Teflon valve and 30 the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting light brown suspension was cooled to room temperature, dodecane (470 μL, GC standard) was added,

and the mixture was filtered through a Celite pad eluting with ethyl acetate. The GC analysis of the filtrate indicated a 38% yield of the product.

Example 56

Preparation of N-(4-methylphenyl)benzamide using 4-chlorotoluene and N,N'-dimethyl-

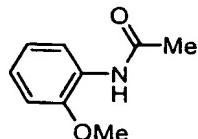
5 **trans-1,2-cyclohexanediamine at 110 °C**



An oven-dried resealable Schlenk tube was charged with CuI (20 mg, 0.105 mmol, 5.1 mol%), benzamide (250 mg, 2.06 mmol), K₂CO₃ (600 mg, 4.34 mmol), evacuated and backfilled with argon. *N,N'*-Dimethyl-*trans*-1,2-cyclohexanediamine (35 µL, 0.222 mmol, 10 11 mol%) and 4-chlorotoluene (1.0 mL, 8.44 mmol) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting dark blue-green suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The light brown filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; 15 hexane-ethyl acetate 2:1; 15 mL fractions). Fractions 4-10 were concentrated, the solid residue was suspended in 10 mL of hexane and filtered to provide 392 mg (90% yield) of the product as fine white needles.

Example 57

N-(2-Methoxyphenyl)acetamide



20

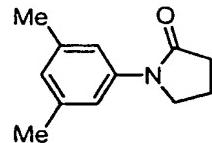
An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 1.0 mol%), acetamide (180 mg, 3.05 mmol), K₃PO₄ (450 mg, 2.12 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (13 µL, 0.108 mmol, 10 mol%), 2-iodoanisole (135 µL, 1.04 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 90 °C for 23 h. The resulting light green suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x15 cm;

hexane-ethyl acetate 2:3; 20 mL fractions). Fractions 10-16 provided 162 mg (94% yield) of the product as white crystals. The ¹H NMR spectrum was in accord with that reported.

Hibbert, F.; Mills, J. F.; Nyburg, S. C.; Parkins, A. W. *J. Chem. Soc., Perkin Trans. I* 1998, 629.

5 **Example 58**

N-(3,5-Dimethylphenyl)-2-pyrrolidinone



- An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 1.0 mol%), K₃PO₄ (450 mg, 2.12 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (13 μL, 0.108 mmol, 10 mol%), 5-iodo-*m*-xylene (150 μL, 1.04 mmol), 2-pyrrolidinone (94 μL, 1.24 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 24 h. The resulting pale yellow suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate 3:2; 20 mL fractions). Fractions 12-23 provided 193 mg (98% yield) of the product as white crystals. ¹H NMR (400 MHz, CDCl₃): δ 7.23 (s, 2H), 6.82 (s, 1H), 3.85 (t, J = 7.1 Hz, 2H), 2.61 (t, J = 8.1 Hz, 2H), 2.34 (s, 6H), 2.16 (tt, J = 8.1, 7.1 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 174.1, 139.2, 138.4, 126.3, 118.0, 49.1, 32.8, 21.5, 18.1. IR (neat, cm⁻¹): 1692, 1596, 1480, 1393, 1333, 1247, 852. Anal. Calcd for C₁₂H₁₅NO: C, 76.16; H, 7.99. Found: C, 76.06; 8.06.

Example 59

Preparation of N-(3,5-dimethylphenyl)-2-pyrrolidinone using copper(II) chloride

- An oven-dried resealable Schlenk tube was charged with CuCl₂ (1.5 mg, 0.0112 mmol, 1.1 mol%), K₃PO₄ (450 mg, 2.12 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (13 μL, 0.108 mmol, 10 mol%), 5-iodo-*m*-xylene (150 μL, 1.04 mmol), 2-pyrrolidinone (94 μL, 1.24 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting pale brown suspension was cooled to room temperature and filtered

through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate 2:3; 15 mL fractions). Fractions 9-18 provided 194 mg (99% yield) of the product as white crystals.

5 **Example 60**

Preparation of N-(3,5-dimethylphenyl)-2-pyrrolidinone using copper powder

An oven-dried resealable Schlenk tube was charged with copper powder (1.5 mg, 0.0236 mmol, 1.1 mol%), K₃PO₄ (900 mg, 4.24 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (26 μL, 0.217 mmol, 10 mol%), 5-iodo-*m*-xylene (300 μL, 2.08 mmol), 2-pyrrolidinone (190 μL, 2.50 mmol) and dioxane (2.0 mL) were added under argon. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting light brown suspension was cooled to room temperature, dodecane (235 μL, GC standard) was added, and the mixture was filtered through a Celite pad eluting with ethyl acetate. The GC analysis of the filtrate indicated a 99% yield of the product.

Example 61

Preparation of N-(3,5-dimethylphenyl)-2-pyrrolidinone under nitrogen

An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 1.0 mol%), K₃PO₄ (450 mg, 2.12 mmol), evacuated and backfilled with nitrogen. *trans*-1,2-Cyclohexanediamine (13 μL, 0.108 mmol, 10 mol%), 5-iodo-*m*-xylene (150 μL, 1.04 mmol), 2-pyrrolidinone (94 μL, 1.24 mmol) and dioxane (1.0 mL) were added under nitrogen. The Schlenk tube was sealed and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting pale brown suspension was cooled to room temperature, dodecane (235 μL, GC standard) was added, and the mixture was filtered through a Celite pad eluting with ethyl acetate. The GC analysis of the filtrate indicated a 99% yield of the product.

Example 62

Preparation of N-(3,5-dimethylphenyl)-2-pyrrolidinone under air

An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 1.0 mol%) and K₃PO₄ (450 mg, 2.12 mmol) under air. *trans*-1,2-Cyclohexanediamine (13 μL, 0.108 mmol, 10 mol%), 5-iodo-*m*-xylene (150 μL, 1.04 mmol), 2-pyrrolidinone (94 μL, 1.24 mmol) and dioxane (1.0 mL) were added under air. The Schlenk tube was sealed and

the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting brown suspension was cooled to room temperature, dodecane (235 µL, GC standard) was added, and the mixture was filtered through a Celite pad eluting with ethyl acetate. The GC analysis of the filtrate indicated a 95% yield of the product.

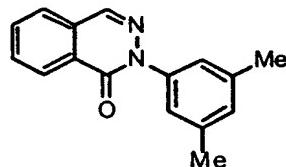
5 **Example 63**

General procedure for the arylation of N-H heterocycles

To a flame-dried resealable Schlenk tube was added CuI, the heterocycle (1.2 mmol) and base (2.1 mmol), was evacuated twice and back-filled with argon. Dodecane (45 µL, 0.20 mmol), ~~t1293~~ alkylhalide, *trans*-1,2-cyclohexanediamine and dioxane were then added 10 successively under argon. The Schlenk tube was sealed and the reaction was stirred with heating via an oil bath at 110 °C for 20 hours. The reaction mixture was cooled to ambient temperature, diluted with 2-3 mL ethyl acetate, and filtered through a plug of silica gel eluting with 10-20 mL of ethyl acetate. The filtrate was concentrated and the resulting residue was purified by column chromatography to provide the purified product.

15 **Example 64**

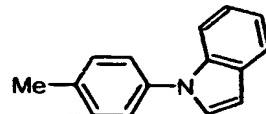
2-(3,5-dimethylphenyl)-1-phthalazinone



Using the general procedure outlined in Example 63, phthalazinone (0.175 g, 1.2 mmol) was coupled with 5-iodo-*m*-xylene (144 µL, 1.00 mmol) using CuI (5.7 mg, 0.030 mmol, 3.0 mol%), Cs₂CO₃ (2.1 mmol), *trans*-1,2-cyclohexanediamine (24 µL, 0.20 mmol, 20 mol%) and dioxane (0.5 mL) to give the crude product. Column chromatography (2x15 cm, hexane:ethyl acetate 10:1) provided 0.225 g (90% yield) of the product as a white solid.
¹H NMR (400 MHz, CDCl₃): δ 8.52 (d, J = 7.3 Hz, 1H), 8.28 (s, 1H), 7.79-7.87 (m, 2H), 7.74-7.47 (m, 1H), 7.25 (bs, 2H), 7.04 (s, 1H), 2.40 (s, 6H).

25 **Example 65**

1-(4-methylphenyl)-indole



Using the general procedure outlined in Example 63, indole (0.117 g, 1.00 mmol) was coupled with 4-bromotoluene (185 µL, 1.50 mmol) using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), K₃PO₄ (2.1 mmol), *trans*-1,2-cyclohexanediamine (24 µL, 0.20 mmol, 20 mol%) and dioxane (1.0 mL) to give the crude product. Column chromatography (2x15 cm, 5 hexane:ethyl acetate 50:1) provided 0.197 g (95% yield) of the product as a white solid. This product was pure by ¹H NMR when compared to the known spectra.

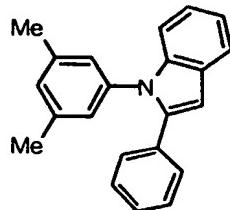
Example 66

Alternative preparation of 1-(4-methylphenyl)-indole

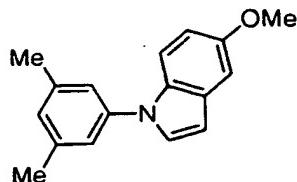
Using the general procedure outlined in Example 63, indole (0.117 g, 1.00 mmol) was coupled with 4-chlorotoluene (1 mL, 8.45 mmol) using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), K₃PO₄ (2.1 mmol) and *trans*-1,2-cyclohexanediamine (24 µL, 0.20 mmol, 20 mol%) to give the crude product. Column chromatography (2 x 15 cm, hexane:ethyl acetate 50:1) provided 0.066 g (32% GC yield) of the product as a white solid. This product was pure by ¹H NMR when compared to the known spectra.

Example 67

1-(4-methylphenyl)-2-phenylindole.



Using the general procedure outlined in Example 63, 2-phenylindole (0.232 g, 1.20 mmol) was coupled with 5-iodo-*m*-xylene (144 µL, 1.00 mmol) using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), K₃PO₄ (2.1 mmol), *trans*-1,2-cyclohexanediamine (24 µL, 0.20 mmol, 20 mol%) and dioxane (0.5 mL) to give the crude product. Column chromatography (2 x 15 cm, hexane:ethyl acetate 10:1) provided 0.220 g (74% yield) of the product as a white solid.
¹H NMR (400 MHz, CDCl₃): δ 7.92 (m, 1H), 7.55 (m, 3H), 7.47 (m, 3H), 7.41 (m, 2H), 7.20 (bs, 1H), 7.13 (bs, 2H), 7.05 (d, 1H, J = 0.6 Hz), 2.52 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 140.63, 139.10, 138.82, 138.29, 132.60, 128.90, 128.70, 128.14, 128.03, 127.12, 125.66, 122.09, 120.48, 120.39, 21.19.

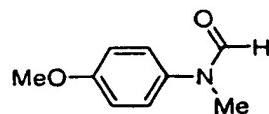
Example 681-(3,5-Dimethylphenyl)-5-methoxyindole

Using the general procedure outlined in Example 63, 5-methoxyindole (0.177 g,

- 5 1.20 mmol) was coupled with 5-iodo-*m*-xylene (144 μ L, 1.00 mmol) using CuI (2.0 mg, 0.010 mmol, 1.0 mol%), K_3PO_4 (2.1 mmol), *trans*-1,2-cyclohexanediamine (12 μ L, 0.10 mmol, 10 mol%) and dioxane (1.0 mL) to give the crude product. Column chromatography (2x15 cm, hexane:ethyl acetate 50:1) provided 0.250 g (100% yield) of the product as a white solid. 1H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, 1H, J = 8.9 Hz), 7.43 (d, 1H, J = 3.2 Hz), 7.32 (d, 1H, J = 3.3 Hz), 7.27 (bs, 2H), 7.12 (bs, 1H), 7.07 (dd, 1H, J = 2.4 Hz and J = 9.0 Hz), 6.75 (d, 1H, J = 2.2 Hz), 4.02 (s, 3H), 2.54 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.33, 139.68, 139.20, 130.93, 129.71, 128.26, 127.78, 121.58, 112.20, 111.37, 102.80, 102.45, 55.58, 21.20.

Example 69

- 15 Preparation of *N*-(4-methoxyphenyl)-*N*-methylformamide using a mixture of *cis*- and *trans*-1,2-cyclohexanediamine



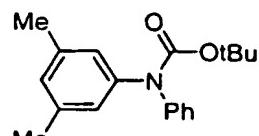
An oven-dried resealable Schlenk tube was charged with CuI (10 mg, 0.0525 mmol,

- 5.0 mol%), Cs_2CO_3 (460 mg, 1.41 mmol), evacuated and backfilled with argon. 1,2-20 Cyclohexanediamine (a mixture of *cis* and *trans* isomers, 13 μ L, 0.106 mmol, 10 mol%), *N*-methylformamide (72 μ L, 1.23 mmol), 4-iodoanisole (245 mg, 1.05 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 110 °C for 22 h. The resulting pale brown suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x10 cm; hexane-ethyl acetate 3:2; 15 mL fractions). Fractions 16-29 provided 158 mg (91% yield) of the product as a colorless oil.

The ^1H NMR spectrum was in accord with that reported by Hoffman. Hoffman et al. *J. Org. Chem.* 1992, 57, 4487.

Example 70

N-tert-Butoxycarbonyl-N-(3,5-dimethylphenyl)aniline

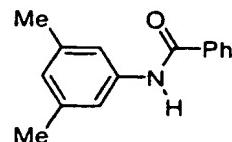


5

- An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 1.0 mol%), *N*-*tert*-butoxycarbonylaniline (200 mg, 1.04 mmol), K_3PO_4 (450 mg, 2.12 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (13 μL , 0.108 mmol, 10 mol%), 5-iodo-*m*-xylene (190 μL , 1.32 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting pale yellow suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate 20:1; 20 mL fractions).
- Fractions 12-20 provided 299 mg (97% yield) of the product as white crystals. ^1H NMR (400 MHz, CDCl_3): δ 7.36-7.30 (m, 2H), 7.27-7.16 (m, 3H), 6.87 (s, 2H), 6.85 (s, 1H), 2.30 (s, 6H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3): δ 153.9, 143.2, 142.7, 138.3, 128.6, 127.5, 126.9, 125.4, 124.8, 80.9, 28.2, 21.2. Anal. Calcd for $\text{C}_{19}\text{H}_{23}\text{NO}_2$: C, 76.74; H, 7.79. Found: C, 76.61; 7.87.

Example 71

Preparation of *N*-(3,5-dimethylphenyl)benzamide at room temperature using *N*-(4-dimethylaminophenyl)-*trans*-1,2-cyclohexane-diamine

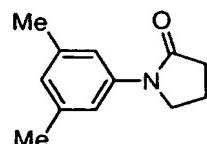


- An oven-dried resealable Schlenk tube was charged with CuI (10 mg, 0.0525 mmol, 2.0 mol%), *N*-(4-dimethylaminophenyl)-*trans*-1,2-cyclohexanediamine (25 mg, 0.107 mmol, 10 mol%), benzamide (150 mg, 1.24 mmol), Cs_2CO_3 (650 mg, 1.99 mmol), evacuated and backfilled with argon. Dioxane (1.0 mL) and 5-iodo-*m*-xylene (150 μL , 1.04

mmol) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at room temperature for 23 h. The resulting light brown suspension was filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The dark purple-brown filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x15 cm; hexane-ethyl acetate 3:1; 15 mL fractions). Fractions 7-15 provided 208 mg (89% yield) of the product as a pale yellow solid.

Example 72

Preparation of N-(3,5-dimethylphenyl)-2-pyrrolidinone using ethylenediamine



10 An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 1.0 mol%), K₃PO₄ (450 mg, 2.12 mmol), evacuated and backfilled with argon. Ethylenediamine (15 µL, 0.224 mmol, 22 mol%), 5-iodo-*m*-xylene (150 µL, 1.04 mmol), 2-pyrrolidinone (94 µL, 1.24 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting pale brown suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x15 cm; hexane-ethyl acetate 2:3; 15 mL fractions). Fractions 9-18 provided 191 mg (97% yield) of the product as white crystals.

15 **Example 73**

Preparation of N-(3,5-dimethylphenyl)-2-pyrrolidinone using ethanolamine

An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 1.0 mol%), K₃PO₄ (450 mg, 2.12 mmol), evacuated and backfilled with argon. Ethanolamine (12 µL, 0.199 mmol, 19 mol%), 5-iodo-*m*-xylene (150 µL, 1.04 mmol), 2-pyrrolidinone (94 µL, 1.24 mmol) and dioxane (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting light brown suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography

on silica gel (2x20 cm; hexane-ethyl acetate 2:3; 15 mL fractions). Fractions 10-18 provided 136 mg (69% yield) of the product as white crystals. The ¹H NMR spectrum was in accord with that reported above.

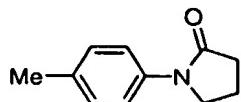
Example 74

5 **Preparation of N-(3,5-dimethylphenyl)-2-pyrrolidinone at 110 °C for 60 min**

- An oven-dried resealable Schlenk tube was charged with CuI (2.0 mg, 0.0105 mmol, 1.0 mol%), K₃PO₄ (450 mg, 2.12 mmol), evacuated and backfilled with argon. *trans*-1,2-Cyclohexanediamine (13 µL, 0.108 mmol, 10 mol%), 5-iodo-*m*-xylene (150 µL, 1.04 mmol), 2-pyrrolidinone (94 µL, 1.24 mmol) and dioxane (1.0 mL) were added under argon.
- 10 The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 110 °C for 60 min. The resulting pale blue suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate 2:3; 15 mL fractions). Fractions 10-20 provided
- 15 176 mg (89% yield) of the product as white crystals. The ¹H NMR spectrum was in accord with that reported above.

Example 75

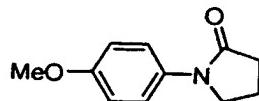
Preparation of N-(4-methylphenyl)-2-pyrrolidinone using 4-chlorotoluene and N,N'-dimethyl-*trans*-1,2-cyclohexanediamine at 130 °C



- 20 An oven-dried resealable Schlenk tube was charged with CuI (20 mg, 0.105 mmol, 5.1 mol%), K₂CO₃ (600 mg, 4.34 mmol), evacuated and backfilled with argon. *N,N'*-Dimethyl-*trans*-1,2-cyclohexanediamine (35 µL, 0.222 mmol, 11 mol%), 2-pyrrolidinone (155 µL, 2.04 mmol) and 4-chlorotoluene (1.0 mL, 8.44 mmol) were added under argon.
- 25 The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 130 °C for 23 h. The resulting dark brown suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x20 cm; hexane-ethyl acetate 1:4; 15 mL fractions). Fractions 7-15 provided
- 30 336 mg (94% yield) of the product as white crystals.

Example 76

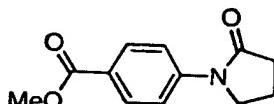
Preparation of N-(4-methoxyphenyl)-2-pyrrolidinone using 4-chloroanisole and N,N'-dimethyl-trans-1,2-cyclohexanediamine at 130 °C



- 5 An oven-dried resealable Schlenk tube was charged with CuI (20 mg, 0.105 mmol, 5.1 mol%), K₂CO₃ (600 mg, 4.34 mmol), evacuated and backfilled with argon. N,N'-Dimethyl-trans-1,2-cyclohexanediamine (35 µL, 0.222 mmol, 11 mol%), 2-pyrrolidinone (155 µL, 2.04 mmol) and 4-chloroanisole (1.0 mL, 8.16 mmol) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred
10 magnetically at 130 °C for 23 h. The resulting dark brown suspension was cooled to room temperature and filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2x15 cm; ethyl acetate; 20 mL fractions). Fractions 7-15 provided 188 mg (48% yield) of the product as a white solid. The ¹H NMR spectrum was in accord with that
15 reported by Easton et al. Easton, C. J.; Pitt, M. J.; Ward, C. M. *Tetrahedron* 1995, 51, 12781.

Example 77

Preparation of N-(4-methoxycarbonylphenyl)-2-pyrrolidinone using methyl 4-chlorobenzoate and N,N'-dimethyl-trans-1,2-cyclohexanediamine at 110 °C



- 20 An oven-dried resealable Schlenk tube was charged with CuI (20 mg, 0.105 mmol, 5.1 mol%), methyl 4-chlorobenzoate (1.40 g, 8.21 mmol), K₂CO₃ (600 mg, 4.34 mmol), briefly evacuated and backfilled with argon. N,N'-Dimethyl-trans-1,2-cyclohexanediamine (35 µL, 0.222 mmol, 11 mol%) and 2-pyrrolidinone (155 µL, 2.04 mmol) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 110 °C for 23 h. The resulting light green-brown suspension was cooled to room temperature and filtered through a 2x0.5 cm pad of silica gel eluting with 30 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash
25

chromatography on silica gel (2x20 cm; hexane-ethyl acetate 1:4; 15 mL fractions). Fractions 10-19 provided 266 mg (59% yield) of the product as white crystals. The ¹H NMR spectrum was in accord with that reported by Atigadda et al. Atigadda, V. R.; Brouillette, W. J.; Duarte, F.; Ali, S. M.; Babu, Y. S.; Bantia, S.; Chand, P.; Chu, N.;
5 Montgomery, J. A.; Walsh, D. A.; Sudbeck, E. A.; Finley, J.; Luo, M.; Air, G. M.; Laver, G. W. *J. Med. Chem.* 1999, 42, 2332.

Example 78

Copper Catalyzed Amination (ethylene glycol system)

General Procedure for Cu-catalyzed amination under argon atmosphere (5 mol% CuI catalyst)
10

Copper(I) iodide (10 mg, 0.05 mmol) and anhydrous fine powder potassium phosphate (425 mg, 2.00 mmol) were put into a Teflon septum screw-capped test tube. The tube was evacuated and back filled with argon. 2-Propanol (1.0 mL), ethylene glycol (111 µL, 2.00 mmol), benzylamine (131 µL, 1.20 mmol) and iodobenzene (112 µL, 1.00 mmol)
15 were added successively by micro-syringe at room temperature. The reaction was heated to 80 °C to give a pale yellow suspension. The reaction was heated to a specified time and then allowed to room temperature. Diethyl ether (2 mL) and water (2 mL) were added to the reaction mixture. The organic layer was analyzed by GC. The reaction mixture was further extracted by diethyl ether (4 x 10 mL). The combined organic phase was washed by
20 water, brine and dried over sodium sulfate or magnesium sulfate. The solvent was removed by rotary evaporation to give the brown residue which was purified by column chromatography on silica gel using a solvent mixture (hexane/ethyl acetate = 20/1) to afford a light yellow liquid as the product.

General procedure for amination under an argon atmosphere (1 mol% CuI catalyst)

25 Copper(I) iodide (2.0 mg, 0.01 mmol) and anhydrous fine powder potassium phosphate (425 mg, 2.00 mmol) were put into a screw-capped test tube with a Teflon septum. The tube was evacuated and back filled with argon three times. 2-Propanol (1.0 mL), ethylene glycol (111 µL, 2.00 mmol), amine (1.20 mmol) and aryl iodide (1.00 mmol) were added successively by micro-syringe at room temperature. The reaction mixture was
30 heated at 80 °C for the specified time and then allowed to reach room temperature. Diethyl ether (2 mL) and water (2 mL) were added to the reaction mixture. The organic layer was analyzed by GC. The reaction mixture was further extracted by diethyl ether (4 x 10 mL).

The combined organic phases were washed by water, brine and dried over sodium sulfate. The solvent was removed by rotary evaporation to give a residue which was purified by column chromatography on silica gel using hexane/ethyl acetate as the eluent to afford the desired product.

5 *General Procedure for Cu-catalyzed amination under air conditions*

Copper(I) iodide (10 mg, 0.05 mmol) and anhydrous fine powder potassium phosphate (425 mg, 2.00 mmol) were put into a Teflon septum screw-capped test tube followed by the addition of 2-propanol (1.0 mL), ethylene glycol (111 μ L, 2.00 mmol), benzylamine (131 μ L, 1.20 mmol) and iodobenzene (112 μ L, 1.00 mmol) by micro-syringe
10 at room temperature. The tube was capped and the reaction was heated to 80 °C to give a yellow suspension. The reaction was heated to a specified time and then allowed to room temperature. Diethyl ether (2 mL) and water (2 mL) were added to the reaction mixture. The organic layer was analyzed by GC. The reaction mixture was further extracted by diethyl ether (4 x 10 mL). The combined organic phase was washed by water, brine and
15 dried over sodium sulfate or magnesium sulfate. The solvent was removed by rotary evaporation to give the brown residue which was purified by column chromatography on silica gel using a solvent mixture (hexane/ethyl acetate = 20/1) to afford a light yellow liquid as the product.

N-(Phenyl)benzylamine (Figure 1, entries 1 and 2)

20 The general procedure under argon or air was followed using copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (425 mg, 2.00 mmol), benzylamine (131 μ L, 1.20 mmol), iodobenzene (112 μ L, 1.00 mmol), ethylene glycol (111 μ L, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.6) afforded *N*-(phenyl)benzylamine (166 mg, 91% isolated yield) as colorless liquid.
25 Spectral data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity: See Apodaca, R.; Xiao, W. *Org. Lett.* 2001, 3, 1745-1748.

4-(N-benzyl)aminoacetophenone (Figure 1, entries 3 and 4)

The general procedure under argón was followed using copper(I) iodide (2.0 mg, 0.01 mmol), K₃PO₄ (425 mg, 2.00 mmol), benzylamine (131 μ L, 1.20 mmol), 4-
30 iodoacetophenone (246 mg, 1.00 mmol), ethylene glycol (111 μ L, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate

= 5/ 1, R_f = 0.2) afforded 4-(*N*-benzyl)aminoacetophenone (203 mg, 90% isolated yield) as yellow solid. Spectral data (1 H NMR) matched with the literature references and GC analysis indicated >95% purity. See Nose, A.; Kudo, T. *Chem. Pharm. Bull.* 1986, 34, 4817-4820.

5 *4-(N-Benzyl)aminobenzonitrile (Figure 1, entry 5)*

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μ L, 1.20 mmol), 4-iodobenzonitrile (229 mg, 1.00 mmol), ethylene glycol (111 μ L, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 5/ 1, R_f = 0.4) afforded 4-(*N*-benzyl)aminobenzonitrile (164 mg, 79% isolated yield) as light yellow solid. Spectral data (1 H NMR) matched with the literature references and GC analysis indicated >95% purity. See Wolfe, J. P.; Tomori, H.; Sadighi, J. P.; Yin, J.; Buchwald, S. L. *J. Org. Chem.* 2000, 65, 1158-1174.

15 *N-(4-Chlorophenyl)benzylamine (Figure 1, entry 6)*

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μ L, 1.20 mmol), 4-chloroiodobenzene (239 mg, 1.00 mmol), ethylene glycol (111 μ L, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 10/ 1, R_f = 0.4) afforded *N*-(4-chlorophenyl)benzylamine (182 mg, 84% isolated yield) as light yellow liquid. The spectral data (1 H NMR) matched with the literature references and GC analysis indicated >95% purity. See Burton, R. D.; Bartberger, M. D.; Zhang, Y.; Eyler, J. R.; Schanze, K. S. *J. Am. Chem. Soc.* 1996, 118, 5655-5664.

20 *N-Benzyl-4-methoxyaniline (Figure 1, entry 7)*

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μ L, 1.20 mmol), 4-iodoanisole (234 mg, 1.00 mmol), ethylene glycol (111 μ L, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 10/ 1, R_f = 0.4) afforded *N*-benzyl-4-methoxyaniline (192 mg, 90% isolated yield) as light yellow solid. The spectral data (1 H NMR) matched with the literature references and GC analysis indicated >95% purity.

25 *N-(4-Tolyl)benzylamine (Figure 1, entry 8)*

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (425 mg, 2.00 mmol), benzylamine (131 µL, 1.20 mmol), 4-iodotoluene (218 mg, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.5) 5 afforded N-(4-tolyl)benzylamine (169 mg, 86% isolated yield) as colorless liquid. The spectral data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity.

5-(N-Benzyl)amino-m-xylene (Figure 1, entries 9 and 10)

The general procedure under argon or air was followed using copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (425 mg, 2.00 mmol), benzylamine (131 µL, 1.20 mmol), 5-iodo-10 m-xylene (144 µL, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.5) afforded 5-(N-benzyl)amino-m-xylene (177 mg, 84% isolated yield) as colorless liquid. The spectral data (¹H NMR) matched with the literature references and GC analysis 15 indicated >95% purity. See Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* 2000, 65, 1144-1157.

N-(3-Bromophenyl)benzylamine (Figure 1, entries 11-13)

The general procedure under argon or air was followed using copper(I) iodide (10 mg, 0.05 mmol or 2.0 mg, 0.01 mmol), K₃PO₄ (425 mg, 2.00 mmol), benzylamine (131 µL, 1.20 mmol), 3-bromoiodobenzene (128 µL, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.4) afforded N-(3-bromophenyl)benzylamine (217 mg, 83% isolated yield) as colorless liquid. The spectral data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity. See Beletskaya, I. P.; Bessmertnykh, A. G.; Guillard, R. *Synlett* 1999, 1459-1461.

N-(3-Cyanophenyl)benzylamine (Figure 1, entry 14)

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (425 mg, 2.00 mmol), benzylamine (131 µL, 1.20 mmol), 3-iodobenzonitrile (229 mg, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 5/ 1, R_f = 0.5) afforded N-(3-cyanophenyl)benzylamine (165 mg, 80% isolated yield) as light yellow

solid. The spectral data (^1H NMR) matched with the literature references and GC analysis indicated >95% purity.

N-(3-Trifluoromethylphenyl)benzylamine (Figure 1, entries 15 and 16)

The general procedure under argon or air was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μL , 1.20 mmol), 3-iodobenzonitrile (144 μl , 1.00 mmol), ethylene glycol (111 μL , 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.4) afforded *N*-(3-trifluoromethylphenyl)benzylamine (229 mg, 91% isolated yield) as colorless liquid. The spectral data (^1H NMR) matched with the literature references and GC analysis indicated >95% purity. See Desmurs, J. R.; Lecouve, J. P.; Kempf, H.; Betremieux, I.; Ratton, S. *New J. Chem.* 1992, 16, 99-106.

N-(3-Methoxyphenyl)benzylamine (Figure 1, entry 17)

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μL , 1.20 mmol), 3-iodoanisole (119 μl , 1.00 mmol), ethylene glycol (111 μL , 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 10/ 1, R_f = 0.4) afforded *N*-(3-methoxyphenyl)benzylamine (171 mg, 80% isolated yield) as white solid. The spectral data (^1H NMR) matched with the literature references and GC analysis indicated >95% purity. See Ali, M. H.; Buchwald, S. L. *J. Org. Chem.* 2001, 66, 2560-2565.

N-(3-Nitrophenyl)benzylamine (Figure 1, entry 18)

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (109 μL , 1.00 mmol), 3-iodonitrobenzene (349 mg, 1.40 mmol), ethylene glycol (111 μL , 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 5/ 1, R_f = 0.4) afforded *N*-(3-nitrophenyl)benzylamine (164 mg, 72% isolated yield) as orange solid. The spectral data (^1H NMR) matched with the literature references and GC analysis indicated >95% purity. See Leardini, R.; Nanni, D.; Tundo, A.; Zanardi, G.; Ruggieri, F. *J. Org. Chem.* 1992, 57, 1842-1848.

30 *N-(3-Tolyl)benzylamine (Figure 1, entry 19)*

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (425 mg, 2.00 mmol), benzylamine (131 µL, 1.20 mmol), 3-iodotoluene (128 µL, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.5) afforded N-(3-tolyl)benzylamine (171 mg, 87% isolated yield) as colorless liquid. The spectral data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity. See Spagnolo, P.; Zanirato, P. *Tetrahedron Lett.* 1987, 28, 961-964.

N-(2-Tolyl)benzylamine (Figure 1, entry 20)

The general procedure under argon was followed using copper(I) iodide (19 mg, 0.10 mmol), K₃PO₄ (425 mg, 2.00 mmol), benzylamine (131 µL, 1.20 mmol), 2-iodotoluene (127 µL, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 1-butanol (1.0 mL) at 100 °C. Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.5) afforded N-(2-tolyl)benzylamine (136 mg, 69% isolated yield) as colorless liquid. The spectral data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity. See Maccarone, E.; Mamo, A.; Torre, M. *J. Org. Chem.* 1979, 44, 1143-1146.

N-(2-Methoxyphenyl)benzylamine (Figure 1, entry 21)

The general procedure under argon was followed using copper(I) iodide (19 mg, 0.10 mmol), K₃PO₄ (425 mg, 2.00 mmol), benzylamine (131 µL, 1.20 mmol), 2-iodoanisole (130 µL, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 1-butanol (1.0 mL) at 100 °C. Column chromatography using a solvent mixture (hexane/ ethyl acetate = 10/ 1, R_f = 0.4) afforded N-(2-methoxyphenyl)benzylamine (149 mg, 70% isolated yield) as colorless liquid. The spectral data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity.

2-(N-Benzyl)aminobenzoic acid (Figure 1, entries 22-24)

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (636 mg, 3.00 mmol), benzylamine (131 µL, 1.20 mmol), 2-iodobenzoic acid (248 mg, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 2-propanol (1.0 mL). After heated for a specified duration, the reaction was allowed to reach room temperature. Water and diluted HCl (10%) was added until ~pH 3. Diethyl ether (2 mL) was added and the organic layer was analyzed by tlc. The reaction mixture was further

extracted by diethyl ether (4 x 10 mL) and the combined organic phase was washed with brine and dried over Na_2SO_4 . The solvent was rotary evaporated and the yellowish-brown residue was purified by column chromatography using a solvent mixture (diethyl ether/ethyl acetate = 1/1, R_f = 0.3) to afford 2-(*N*-benzyl)aminobenzoic acid (161 mg, 71% isolated yield) as light yellow solid. For aryl bromide substrate: copper(I) iodide (19 mg, 0.10 mmol), K_3PO_4 (636 mg, 3.00 mmol), benzylamine (131 μl , 1.20 mmol), 2-bromobenzoic acid (201 mg, 1.00 mmol), ethylene glycol (111 μl , 2.00 mmol) and 1-butanol (1.0 mL) was used and heated to 100 °C. The above workup procedures was followed and obtained 2-(*N*-benzyl)aminobenzoic acid (120 mg, 53% isolated yield) as light yellow solid. For aryl chloride substrate: copper(I) iodide (19 mg, 0.10 mmol), K_3PO_4 (636 mg, 3.00 mmol), benzylamine (131 μl , 1.20 mmol), 2-chlorobenzoic acid (157 mg, 1.00 mmol), ethylene glycol (111 μl , 2.00 mmol) and 1-butanol (1.0 mL) was used and heated to 100 °C. The above workup procedures was followed and obtained 2-(*N*-benzyl)aminobenzoic acid (109 mg, 48% isolated yield) as light yellow solid. The spectral data (^1H NMR) matched with the literature references and indicated >95% purity. See Chang, M. R.; Takeuchi, Y.; Hashigaki, K.; Yamato, M. *Heterocycles* 1992, 33, 147-152. Moore, J. A.; Sutherland, G. J.; Sowerby, R.; Kelly, E. G.; Palermo, S.; Webster, W. *J. Org. Chem.* 1969, 34, 887-892.

2-(*N*-Benzyl)aminobenzylalcohol (Figure 1, entry 25)

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.5 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μL , 1.20 mmol), 2-iodobenzylalcohol (234 mg, 1.00 mmol), ethylene glycol (111 μL , 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 4/1, R_f = 0.3) afforded 2-(*N*-benzyl)aminobenzylalcohol (203 mg, 95% isolated yield) as off-white solid. The spectral data (^1H NMR) matched with the literature references and GC analysis indicated >95% purity. See Coppola, G. A. *J. Heterocycl. Chem.* 1986, 23, 223-224.

4-(*N*-Benzyl)aminoaniline (Figure 1, entry 26)

The general procedure under argon was followed using copper(I) iodide (19 mg, 0.10 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (218 μL , 2.0 mmol), 4-iodoaniline (219 mg, 1.00 mmol), ethylene glycol (111 μL , 2.00 mmol) and 2-propanol (1.0 mL) at 90

°C. Column chromatography using a solvent gradient (hexane/ ethyl acetate = 2/ 1 to 1/ 1, R_f = 0.2) afforded 4-(N-benzyl)aminoaniline (101 mg, 51% isolated yield) as brown solid. The spectral data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity. See Araki, T.; Tsukube, H. *J. Polym. Sci., Polym. Lett. Ed.* 1979, 5 17, 501-505.

Ethyl 4-(N-benzyl)aminobenzoate (Figure 1, entry 27)

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (425 mg, 2.00 mmol), benzylamine (131 µL, 1.20 mmol), ethyl 4-iodobenzoate (167 µL, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and ethanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 5/ 1, R_f = 0.4) afforded ethyl 4-(N-benzyl)aminobenzoate (113 mg, 50% isolated yield) as light yellow solid. The spectral data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity. See Albright, J. D.; DeVries, V. G.; Largis, E. E.; Miner, T. G. Reich, M. F.; Schaffer, S.; Shepherd, R. G.; Upeslacis, J. *J. Med. Chem.* 1983, 26, 1378-15 1393; and Onaka, M.; Umezono, A.; Kawai, M.; Izumi, Y. *J. Chem. Soc., Chem. Commun.* 1985, 1202-1203.

N-(1-Naphthyl)benzylamine (Figure 1, entry 28)

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (425 mg, 2.00 mmol), benzylamine (131 µL, 1.20 mmol), 1-iodonaphthlene (146 µL, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.4) afforded *N*-(1-naphthyl)benzylamine (163 mg, 70% isolated yield) as light yellow solid. The spectral data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity. See Janin, Y. L.; Bisagni, E. *Synthesis* 1993, 57-59.

N-(Phenyl)hexylamine (Figure 2, entries 2-4)

The general procedure under argon or air was followed using copper(I) iodide (10 mg, 0.05 mmol or 2.0 mg, 0.01 mmol), K₃PO₄ (425 mg, 2.00 mmol), hexylamine (159 µL, 1.20 mmol), iodobenzene (112 µL, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.5) afforded *N*-(phenyl)hexylamine (152 mg, 86% isolated yield) as colorless liquid. The spectral data (¹H NMR) matched with the literature references and GC analysis

indicated >95% purity. See Bomann, M. D.; Guch, I. C.; DiMare, M. *J. Org. Chem.* 1995, 60, 5995-5996.

N-(2-Methoxyethyl)aniline (Figure 2, entries 5-7)

The general procedure under argon or air was followed using copper(I) iodide (10 mg, 0.05 mmol or 2.0 mg, 0.01 mmol), K₃PO₄ (425 mg, 2.00 mmol), 2-methoxyethylamine (104 μL, 1.20 mmol), iodobenzene (112 μL, 1.00 mmol), ethylene glycol (111 μL, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ethyl acetate = 10/ 1, R_f = 0.2) afforded *N*-(2-methoxyethyl)aniline (138 mg, 91% isolated yield) as colorless liquid. The spectral data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity. See Fancher, L. W.; Gless, R. D., Jr.; Wong, R. Y. *Tetrahedron Lett.* 1988, 29, 5095-5098.

N-(Phenyl)-α-methylbenzylamine (Figure 2, entry 8)

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (425 mg, 2.00 mmol), α-methylbenzylamine (155 μL, 1.20 mmol), iodobenzene (112 μL, 1.00 mmol), ethylene glycol (111 μL, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ethyl acetate = 20/ 1, R_f = 0.5) afforded *N*-(phenyl)-α-methylbenzylamine (144 mg, 73% isolated yield) as colorless liquid. HPLC conditions: (column: Daicel OD-H; solvent: 10% ¹PrOH in hexane; flow rate: 0.7 mL/ min; UV lamp: 254 nm; retention time: 6.01, 6.78 min). The spectral data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity. See Kainz, S.; Brinkmann, A.; Leitner, W.; Pfaltz, A. *J. Am. Chem. Soc.* 1999, 121, 6421-6429.

(R)-N-(Phenyl)-α-methylbenzylamine (Figure 2, entry 9)

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (425 mg, 2.00 mmol), (R)-α-methylbenzylamine (155 μL, 1.20 mmol), iodobenzene (112 μL, 1.00 mmol), ethylene glycol (111 μL, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ethyl acetate = 20/ 1, R_f = 0.5) afforded (R)-*N*-(phenyl)-α-methylbenzylamine (150 mg, 76% isolated yield, 99% ee) as colorless liquid. HPLC conditions: (column: Daicel OD-H; solvent: 10% ¹PrOH in hexane; flow rate: 0.7 mL/ min; UV lamp: 254 nm; retention time: 6.74 min). The spectral

data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity.

N-Methyl-N-phenylbenzylamine (Figure 2, entry 10)

The general procedure under argon was followed using copper(I) iodide (19 mg, 5 0.10 mmol), K₃PO₄ (425 mg, 2.00 mmol), *N*-methylbenzylamine (155 µL, 1.20 mmol), iodobenzene (112 µL, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 1-butanol (1.0 mL) at 90 °C. Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.5) afforded *N*-methyl-*N*-phenylbenzylamine (146 mg, 74% isolated yield) as colorless liquid. The spectral data (¹H NMR) matched with the literature references and GC 10 analysis indicated >95% purity. See Brenner, E.; Schneider, R.; Fort, Y. *Tetrahedron* 1999, 55, 12829-12842.

N-(Phenyl)pyrrolidine (Figure 2, entries 11-13)

The general procedure under argon or air was followed using copper(I) iodide (10 mg, 0.05 mmol or 2.0 mg, 0.01 mmol), K₃PO₄ (425 mg, 2.00 mmol), pyrrolidine (100 µL, 15 1.20 mmol), iodobenzene (112 µL, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.4) afforded *N*-(phenyl)pyrrolidine (133 mg, 90% isolated yield) as colorless liquid. The spectral data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity. See Ishikawa, T.; Uedo, E.; Tani, R.; Saito, S. *J. Org. Chem.* 2001, 20 66, 186-191.

N-(Phenyl)piperidine (Figure 2, entry 14)

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (425 mg, 2.00 mmol), piperidine (119 µL, 1.20 mmol), iodobenzene (112 µL, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 2-propanol (1.0 mL). 25 Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.4) afforded *N*-(phenyl)piperidine (129 mg, 80% isolated yield) as colorless liquid. The spectral data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity. See Beller, M.; Breindl, C.; Riermeier, T. H.; Tillack, A. *J. Org. Chem.* 2001, 66, 1403-1412; and Li, G. Y. *Angew. Chem., Int. Ed.* 2001, 40, 1513-1516.

30 *N-(Phenyl)morpholine (Figure 2, entry 15)*

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (425 mg, 2.00 mmol), morpholine (130 µL, 1.50 mmol), iodobenzene (112 µL, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 2-propanol (1.0 mL).

Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.2) 5 afforded N-(phenyl)morpholine (124 mg, 76% isolated yield) as colorless liquid. The spectral data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity. See Desmarests, C.; Schneider, R.; Fort, Y. *Tetrahedron Lett.* 2000, 41, 2875-2879.

N-phenyl-N'-(methyl)piperazine (Figure 2, entry 16)

10 The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (425 mg, 2.00 mmol), N-(methyl)piperazine (166 µL, 1.50 mmol), iodobenzene (112 µL, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.1) afforded N-phenyl-N'-(methyl)piperazine (125 mg, 71% isolated yield) as 15 colorless liquid. The spectral data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity.

N-Phenyl-L-proline (Figure 2, entry 17)

20 The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (425 mg, 2.00 mmol), L-proline (138 mg, 1.20 mmol), iodobenzene (112 µL, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 2-propanol (1.0 mL). After heated for a specified duration, the reaction was allowed to reach room temperature. Water and diluted HCl (10%) was added until ~pH 3. Diethyl ether (2 mL) was added and the organic layer was analyzed by tlc. The reaction mixture was further extracted by diethyl ether (4 x 10 mL) and the combined organic phase was washed with brine and dried over 25 Na₂SO₄. The solvent was rotary evaporated and the yellowish-brown residue was purified by column chromatography using a solvent mixture (diethyl ether/ ethyl acetate = 1/ 1, R_f = 0.2) to afford N-phenyl-L-proline (134 mg, 70% isolated yield) as light yellow solid. The spectral data (¹H NMR) matched with the literature references and indicated >95% purity. See Ma, D.; Zhang, Y.; Yao, J.; Wu, S.; Tao, F. *J. Am. Chem. Soc.* 1998, 120, 12459-12467.

30 *N-(Phenyl)aniline (Figure 2, entry 18)*

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (425 mg, 2.00 mmol), aniline (109 µL, 1.20 mmol), iodobenzene (112 µL, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 2-propanol (1.0 mL) at 90 °C. Column chromatography using a solvent mixture (hexane/ ethyl acetate = 5/ 1, R_f = 0.4) 5 afforded N-(phenyl)aniline (69 mg, 41% isolated yield) as light yellow solid. The spectral data (¹H NMR) matched with the literature references and GC analysis indicated >95% purity.

N-(Phenyl)-2-pyrrolidinone (Figure 2, entry 21)

The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (425 mg, 2.00 mmol), 2-pyrrolidinone (91 µL, 1.20 mmol), iodobenzene (112 µL, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 2-propanol (1.0 mL) at 90 °C. Column chromatography using a solvent mixture (hexane/ ethyl acetate = 1/ 1) afforded N-(phenyl)-2-pyrrolidinone (80 mg, 50% isolated yield) as white solid. The spectral data (¹H NMR) matched with the literature references and GC analysis indicated 15 >95% purity. See Yin, J.; Buchwald, S. L. *Org. Lett.* **2000**, 2, 1101-1104; and Kang, S.-K.; Lee, S.-H.; Lee, D. *Synlett* **2000**, 1022-1024.

N-(4-Methoxyphenyl)cyclohexylamine (Figure 3, entry 1)

An oven-dried resealable 15 mL Schlenk tube was charged with CuI (9.5 mg, 0.0499 mmol, 5.0 mol%), K₃PO₄ (440 mg, 2.07 mmol), evacuated and backfilled with argon. 20 Cyclohexylamine (144 µL, 1.26 mmol), ethylene glycol (0.11 mL, 1.97 mmol), and a solution of 4-iodoanisole (235 mg, 1.00 mmol) in 1-butanol (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 100 °C for 14 h. The resulting thick, green-brown suspension was allowed to reach room temperature, poured into a solution of 30% aq ammonia (1 mL) in water (20 mL), and extracted with 3×15 mL of CH₂Cl₂. The colorless organic phase was dried (Na₂SO₄), concentrated, and the residue was purified by flash chromatography on 25 silica gel (2×15 cm; hexane-ethyl acetate 5:1; 15 mL fractions). Fractions 9-17 provided 143 mg (70% yield) of the product as white crystals. ¹H NMR (400 MHz, CDCl₃): δ 6.79-6.72 (m, 2H), 6.60-6.53 (m, 2H), 3.74 (s, 3H), 3.22 (br s, 1H), 3.16 (tt, J = 10.2, 3.6 Hz, 1H), 2.10-1.98 (m, 2H), 1.80-1.69 (m, 2H), 1.68-1.58 (m, 1H), 1.40-1.04 (m, 5H). ¹³C 30 NMR (100 MHz, CDCl₃): δ 151.8, 141.6, 114.8, 114.7, 55.8, 52.7, 33.6, 25.9, 25.0. IR

(neat, cm^{-1}): 3388, 1509, 1239, 1038, 818. Anal. Calcd. for $\text{C}_{13}\text{H}_{19}\text{NO}$: C, 76.06; H, 9.33. Found: C, 76.00; H, 9.32.

5-(4-Methoxyphenylamino)-1-pentanol (Figure 3, entry 2)

An oven-dried resealable 15 mL Schlenk tube was charged with CuI (9.5 mg, 0.0499 mmol, 5.0 mol%), K_3PO_4 (440 mg, 2.07 mmol), evacuated and backfilled with argon. 5-Amino-1-pentanol (135 μL , 1.24 mmol), ethylene glycol (0.11 mL, 1.97 mmol), and a solution of 4-iodoanisole (235 mg, 1.00 mmol) in 1-butanol (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 100 °C for 14 h. The resulting thick, yellow-brown suspension was allowed to reach room temperature, poured into a solution of 30% aq ammonia (1 mL) in water (20 mL), and extracted with 3×15 mL of CH_2Cl_2 . The organic phase was dried (Na_2SO_4), concentrated, and the residue was purified by flash chromatography on silica gel (2×15 cm; ethyl acetate; 15 mL fractions). Fractions 6-15 provided 177 mg (85% yield) of the product as a pale tan oil. ^1H NMR (400 MHz, CDCl_3): δ 6.80-6.74 (m, 2H), 6.60-6.54 (m, 2H), 3.74 (s, 3H), 3.65 (t, J = 6.4 Hz, 2H), 3.07 (t, J = 7.0 Hz, 2H), 2.5 (br s, 2H), 1.68-1.55 (m, 4H), 1.52-1.41 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 151.9, 142.6, 114.8, 114.0, 62.7, 55.8, 44.9, 32.4, 29.4, 23.3. IR (neat, cm^{-1}): 3350, 1511, 1233, 1036, 820. Anal. Calcd. for $\text{C}_{12}\text{H}_{19}\text{NO}_2$: C, 68.87; H, 9.15. Found: C, 68.93; H, 9.12.

N-(3-Methylphenyl)-2-(1-cyclohexenyl)ethylamine (Figure 3, entry 3)

An oven-dried resealable 15 mL Schlenk tube was charged with CuI (9.6 mg, 0.0504 mmol, 5.0 mol%), K_3PO_4 (440 mg, 2.07 mmol), evacuated and backfilled with argon. 3-Iodotoluene (130 μL , 1.01 mmol), 2-(1-cyclohexenyl)ethylamine (170 μL , 1.22 mmol), ethylene glycol (115 μL , 1.97 mmol), and isopropyl alcohol (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 80 °C for 22 h. The resulting thick, green-brown suspension was allowed to reach room temperature, poured into a solution of 30% aq ammonia (1 mL) in water (20 mL), and extracted with 3×15 mL of CH_2Cl_2 . The organic phase was dried (Na_2SO_4), concentrated, and the residue was purified by flash chromatography on silica gel (2×15 cm; hexane-ethyl acetate 50:1; 15 mL fractions). Fractions 12-17 provided 189 mg (87% yield) of the product as a colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 7.06 (t, J = 7.4 Hz, 1H), 6.52 (d, J = 7.4 Hz, 1H), 6.46-6.39 (m, 2H), 5.53 (m, 1H), 3.57 (br s, 1H), 3.14

(t, $J = 6.8$ Hz, 2H), 2.30-2.22 (m, 5H), 2.07-1.98 (m, 2H), 1.97-1.90 (m, 2H), 1.67-1.52 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3): δ 148.5, 138.9, 134.9, 129.1, 123.5, 118.1, 113.6, 109.9, 41.4, 37.6, 27.8, 25.2, 22.8, 22.4, 21.6. IR (neat, cm^{-1}): 3406, 1603, 1590, 1509, 1492, 1478, 1328, 766, 691. Anal. Calcd. for $\text{C}_{15}\text{H}_{21}\text{N}$: C, 83.67; H, 9.83. Found: C, 5 83.82; H, 9.84.

2-(4-Aminophenyl)-N-(3,5-dimethylphenyl)ethylamine (Figure 3, entry 4)

An oven-dried resealable 15 mL Schlenk tube was charged with CuI (9.6 mg, 0.0504 mmol, 5.0 mol%), K_3PO_4 (440 mg, 2.07 mmol), evacuated and backfilled with argon. 5-Iodo-*m*-xylene (145 μL , 1.00 mmol), 2-(4-aminophenyl)ethylamine (160 μL , 1.21 mmol), 10 ethylene glycol (115 μL , 2.06 mmol), and isopropyl alcohol (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 80 °C for 22 h. The resulting thick, gray-brown suspension was allowed to reach room temperature, poured into a solution of 30% aq ammonia (1 mL) in water (20 mL), and extracted with 3×15 mL of CH_2Cl_2 . The yellow-brown organic phase 15 was dried (Na_2SO_4), concentrated, and the residue was purified by flash chromatography on silica gel (2×20 cm; hexane-ethyl acetate 3:2; 15 mL fractions). Fractions 9-18 were concentrated and the residue was recrystallized from hexanes (5 mL) to give 167 mg (69% yield) of the desired product as large white needles. ^1H NMR (400 MHz, CDCl_3): δ 7.04-6.97 (m, 2H), 6.67-6.61 (m, 2H), 6.36 (s, 1H), 6.24 (s, 2H), 3.65-3.50 (br m, 3H), 3.30 (t, $J = 6.8$ Hz, 2H), 2.79 (t, $J = 7.0$ Hz, 2H), 2.23 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 148.2, 144.7, 138.8, 129.5, 129.2, 119.3, 115.3, 110.9, 45.3, 34.6, 21.5. IR (neat, cm^{-1}): 3361, 3215, 1600, 1515, 1472, 1337, 1273, 1181, 820.

N-(4-Methylphenyl)-N'-(3-(4-methylphenylamino)propyl)-1,4-butanediamine (Figure 3, entry 6)

25 An oven-dried resealable 15 mL Schlenk tube was charged with CuI (9.6 mg, 0.0504 mmol), 4-iodotoluene (260 mg, 1.19 mmol), K_3PO_4 (440 mg, 2.07 mmol), evacuated and backfilled with argon. *N*-(3-Aminopropyl)-1,4-butanediamine (79 μL , 0.503 mmol), ethylene glycol (115 μL , 2.06 mmol), and isopropyl alcohol (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was 30 stirred magnetically at 80 °C for 23 h. The resulting thick, gray-brown suspension was allowed to reach room temperature, poured into a solution of 30% aq ammonia (1 mL) in

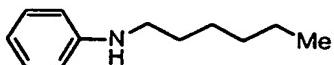
water (20 mL), and extracted with 3×15 mL of CH₂Cl₂. The organic phase was dried (Na₂SO₄), concentrated, and the residue was purified by flash chromatography on silica gel (2×15 cm; dichloromethane - dichloromethane saturated with 30% aq ammonia - methanol 30:20:2; 15 mL fractions). Fractions 12-24 were concentrated and the residue was

5 recrystallized from hexanes (2 mL) to give 119 mg (73% yield) of the desired product as fine white crystals. ¹H NMR (400 MHz, CDCl₃): δ 6.98 (d, *J* = 8.4 Hz, 4H), 6.56-6.50 (m, 4H), 4.04 (br s, 1H), 3.56 (br s, 1H), 3.17 (t, *J* = 6.6 Hz, 2H), 3.11 (t, *J* = 6.6 Hz, 2H), 2.74 (t, *J* = 6.6 Hz, 2H), 2.64 (t, *J* = 6.9 Hz, 2H), 2.23 (s, 6H), 1.79 (quintet, *J* = 6.6 Hz, 2H), 1.70-1.54 (m, 4H), 0.95 (br s, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 146.3, 146.1, 129.7, 126.3, 112.89, 112.85, 49.8, 48.5, 44.2, 43.3, 29.6, 27.8, 27.3, 20.4.

10

Example 79

Preparation of N-phenylhexylamine using 2-phenylphenol as the ligand and toluene as the solvent



15 A screw cap test tube was purged with nitrogen and charged with CuI (9.5 mg, 0.0499 mmol, 5.0 mol%), 2-phenylphenol (34 mg, 0.200 mmol, 20 mol%), and K₃PO₄ (440 mg, 2.07 mmol). The test tube was capped and brought into a nitrogen filled glovebox, the cap being removed immediately before evacuating the antechamber. The test tube was sealed with an open top screw cap lined with a Teflon-faced silicone rubber septum and

20 then removed from the glovebox. Bromobenzene (105 μL, 1.00 mmol), *n*-hexylamine (160 μL, 1.21 mmol), and toluene (1.0 mL) were added using syringes. After the reaction mixture was stirred magnetically at 100 °C for 23 h, the resulting dark brown suspension was allowed to reach room temperature, poured into a solution of 30% aq ammonia (1 mL) in water (20 mL), and extracted with 3×15 mL of CH₂Cl₂. The light brown organic phase

25 was dried (Na₂SO₄), concentrated, and the residue was purified by flash chromatography on silica gel (2×15 cm; hexane-dichloromethane 2:1; 15 mL fractions). Fractions 14-25 provided 112 mg (63% yield) of the desired product as a colorless liquid. The ¹H NMR spectrum matched the one reported. Barluenga, J.; Fananas, F. J.; Villamana, J.; Yus, M. J. *Org. Chem.* 1982, 47, 1560.

Example 80Preparation of N-phenylhexylamine using 2-phenylphenol as the ligand and dioxane as the solvent

A screw cap test tube was purged with nitrogen and charged with CuI (9.5 mg, 5 0.0499 mmol, 5.0 mol%), 2-phenylphenol (34 mg, 0.200 mmol, 20 mol%), and K₃PO₄ (440 mg, 2.07 mmol). The test tube was capped and brought into a nitrogen filled glovebox, the cap being removed immediately before evacuating the antechamber. The test tube was sealed with an open top screw cap lined with a Teflon-faced silicone rubber septum and then removed from the glovebox. Bromobenzene (105 µL, 1.00 mmol), *n*-hexylamine (160 10 µL, 1.21 mmol), and dioxane (1.0 mL) were added using syringes. After the reaction mixture was stirred magnetically at 100 °C for 23 h, the resulting brown suspension was allowed to reach room temperature and was then diluted with ether (2 mL) and water (1 mL). Dodecane (230 µL; internal GC standard) was added and a sample of the top (organic) layer was analyzed by GC revealing 74% conversion of bromobenzene and 60% 15 yield of the desired product.

Example 81Preparation of N-phenylhexylamine using 2-phenylphenol as the ligand and no solvent

A screw cap test tube was purged with nitrogen and charged with CuI (9.5 mg, 0.0499 mmol, 5.0 mol%), 2-phenylphenol (34 mg, 0.200 mmol, 20 mol%), and K₃PO₄ (440 20 mg, 2.07 mmol). The test tube was capped and brought into a nitrogen filled glovebox, the cap being removed immediately before evacuating the antechamber. The test tube was sealed with an open top screw cap lined with a Teflon-faced silicone rubber septum and then removed from the glovebox. Bromobenzene (105 µL, 1.00 mmol) and *n*-hexylamine (0.94 mL, 7.12 mmol) were added using syringes. After the reaction mixture was stirred 25 magnetically at 100 °C for 23 h, the resulting brown suspension was allowed to reach room temperature, poured into a solution of 30% aq ammonia (1 mL) in water (20 mL), and extracted with 3×15 mL of CH₂Cl₂. The light brown organic phase was dried (Na₂SO₄), concentrated, and the residue was purified by flash chromatography on silica gel (2×20 cm; hexane-dichloromethane 2:1; 15 mL fractions). Fractions 13–25 provided 161 mg (91% 30 yield) of the desired product as a colorless liquid. The ¹H NMR spectrum matched the one reported. Barluenga, J.; Fananas, F. J.; Villamana, J.; Yus, M. *J. Org. Chem.* 1982, 47, 1560.

Example 82**Preparation of N-phenylhexylamine from phenyl trifluoromethanesulfonate**

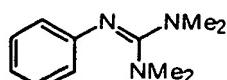
An oven-dried resealable 15 mL Schlenk tube was charged with CuI (19.5 mg, 0.102 mmol, 10 mol%), 2-phenylphenol (86 mg, 0.505 mmol, 50 mol%), K₃PO₄ (440 mg, 2.07 mmol), evacuated and backfilled with argon. *n*-Hexylamine (135 µL, 1.02 mmol) and phenyl trifluoromethanesulfonate (0.98 mL, 6.05 mmol) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 120 °C for 23 h. The resulting thick, brown suspension was allowed to reach room temperature and was then diluted with ethyl acetate (2 mL). Dodecane (230 µL; internal GC standard) was added and a sample of the supernatant solution was analyzed by GC revealing 1% yield of the desired product. The identity of the product was confirmed by GC-MS (signal at 177 m/z).

Example 83**Preparation of N-(4-methylphenyl)hexylamine from 4-chlorotoluene**

An oven-dried resealable 15 mL Schlenk tube was charged with CuI (19.5 mg, 0.102 mmol, 10 mol%), 2-phenylphenol (86 mg, 0.505 mmol, 50 mol%), K₃PO₄ (440 mg, 2.07 mmol), evacuated and backfilled with argon. *n*-Hexylamine (135 µL, 1.02 mmol) and 4-chlorotoluene (0.95 mL, 8.01 mmol) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 120 °C for 23 h. The resulting brown suspension was allowed to reach room temperature and filtered through a 0.5×1 cm silica plug eluting with dichloromethane (10 mL). The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2×20 cm; hexane-dichloromethane 2:1; 15 mL fractions). Fractions 12-23 were concentrated and the residue was further purified by flash chromatography on silica gel (2×15 cm; hexane-ethyl acetate 20:1; 15 mL fractions). Fractions 9-15 provided 85 mg (44% yield) of the pure desired product as large colorless crystals. The ¹H and ¹³C NMR spectra were in accord with those reported. Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* 1996, 61, 1133.

Example 84

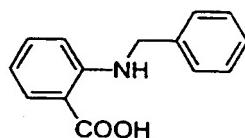
30 **Preparation of N-phenyl-N',N',N'',N''-tetramethylguanidine using 2-phenylphenol as the ligand in toluene**



A 15 mL Schlenk tube was charged with CuI (9.6 mg, 0.0504 mmol, 5.0 mol%), 2-phenylphenol (34 mg, 0.200 mmol, 20 mol%), K_3PO_4 (430 mg, 2.03 mmol), evacuated and backfilled with argon. Iodobenzene (112 μL , 1.00 mmol), *N,N,N',N'*-tetramethylguanidine 5 (190 μL , 1.51 mmol) and toluene (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and stirred at 110 °C for 23 h. The resulting pale brown suspension was allowed to reach room temperature and then filtered through a Celite plug eluting with dichloromethane. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2×15 cm; methanol-dichloromethane (saturated with 10 30% aq NH_3) 1:5, 20 mL fractions). Fractions 26–43 provided 159 mg (83% yield) of the desired product.

Example 85

2-(*N*-Benzyl)aminobenzoic acid



15 ***Aryl bromide substrate***

Copper(I) iodide (19 mg, 0.10 mmol), K_3PO_4 (636 mg, 3.00 mmol) and 2-bromobenzoic acid (201 mg, 1.00 mmol) were put into a screw-capped test tube with a Teflon septum. The tube was evacuated and back-filled with argon three times. 1-Butanol (1.0 mL), ethylene glycol (111 μL , 2.00 mmol) and benzylamine (131 μL , 1.20 mmol) were 20 added by micro-syringes. The reaction was heated at 100 °C for 48 hours to give a pale blue suspension. After the reaction mixture was allowed to reach room temperature, water and diluted HCl (10%) were added until ~pH 3. Diethyl ether (2 mL) was added and the organic layer was analyzed by tlc. The reaction mixture was further extracted by diethyl ether (4 x 10 mL) and the combined organic phases were washed with brine and dried over 25 Na_2SO_4 . Column chromatography on silica gel eluting with diethyl ether/ethyl acetate = 1/1 provided 2-(*N*-benzyl)aminobenzoic acid (120 mg, 53% isolated yield) as a light yellow solid.

Aryl chloride substrate

Copper(I) iodide (19 mg, 0.10 mmol), K₃PO₄ (636 mg, 3.00 mmol), benzylamine (131 µL, 1.20 mmol), 2-chlorobenzoic acid (157 mg, 1.00 mmol), ethylene glycol (111 µL, 2.00 mmol) and 1-butanol (1.0 mL) were used and heated to 100 °C for 72 hours. The 5 above workup procedure was followed and gave 2-(*N*-benzyl)aminobenzoic acid (109 mg, 48% isolated yield) as a light yellow solid.

Aryl iodide substrate

Copper(I) iodide (10 mg, 0.05 mmol), K₃PO₄ (636 mg, 3.00 mmol), benzylamine (131 µL, 1.20 mmol), 2-iodobenzoic acid (248 mg, 1.00 mmol), ethylene glycol (111 µL, 10 2.00 mmol) and 2-propanol (1.0 mL) were used and heated at 80 °C for 18 hours. The above workup procedure was followed and gave 2-(*N*-benzyl)aminobenzoic acid (161 mg, 71% isolated yield) as a light yellow solid.

Example 86General procedure for amination of bromobenzene in toluene under an Ar atmosphere

15 Copper (I) iodide (10 mg, 0.05 mmol, 5 mol%), anhydrous fine powder potassium phosphate (425 mg, 2.0 mmol) and the substituted phenol (0.2 mmol, 20 mol%) were put into a screw-capped test tube with a Teflon septum. The tube was evacuated and back-filled with argon (3 cycles). Anhydrous toluene (1.0 mL), bromobenzene (105 µL, 1.0 mmol) and *n*-hexylamine (158 µL, 1.2 mmol) were added by micro-syringe at room temperature. The 20 reaction mixture was heated at 100 °C for 18 hours. The reaction mixture was then allowed to reach room temperature. Diethyl ether (2 mL), water (2 mL) and dodecane (internal standard, 227 µL) were added. The organic layer was analyzed by GC to determine the yield of *N*-phenylhexylamine. Examples using the above procedure are tabulated in Figure 4.

Example 87Preparation of *N*-phenylhexylamine using 2,6-dimethylphenol as the ligand and DMF as the solvent

25 Copper (I) iodide (10 mg, 0.05 mmol, 5 mol%), anhydrous fine powder potassium phosphate (425 mg, 2.0 mmol) and 2,6-dimethylphenol (24 mg, 0.2 mmol, 20 mol%) were put into a screw-capped test tube with a Teflon septum. The tube was evacuated and back-filled with argon (3 cycles). Anhydrous DMF (1.0 mL), bromobenzene (105 µL, 1.0 mmol) 30 and *n*-hexylamine (158 µL, 1.2 mmol) were added by micro-syringe at room temperature.

The reaction mixture was heated at 100 °C for 18 hours. The reaction mixture was then allowed to reach room temperature. Diethyl ether (2 mL), water (2 mL) and dodecane (internal standard, 227 µL) were added. The organic layer was analyzed by GC to give 48% GC yield of *N*-phenylhexylamine.

5 Example 88

Preparation of *N*-phenylhexylamine using 2,6-dimethylphenol as the ligand and no solvent

Copper (I) iodide (10 mg, 0.05 mmol, 5 mol%), anhydrous fine powder potassium phosphate (425 mg, 2.0 mmol) and 2,6-dimethylphenol (24 mg, 0.2 mmol, 20 mol%) were put into a screw-capped test tube with a Teflon septum. The tube was evacuated and back-filled with argon (3 cycles). Bromobenzene (105 µL, 1.0 mmol) and *n*-hexylamine (1.05 mL, 8.0 mmol) were added by micro-syringe at room temperature. The reaction mixture was heated at 100 °C for 18 hours. The reaction mixture was then allowed to reach room temperature. Diethyl ether (2 mL), water (2 mL) and dodecane (internal standard, 227 µL) were added. The organic layer was analyzed by GC to give 100% conversion of 10 bromobenzene. The aqueous phase was further extracted with diethyl ether (4 x 10 mL). The combined organic phases were washed with water, brine and dried over sodium sulfate. The solvent was removed by rotary evaporation and the residue was purified by column chromatography on silica gel eluting with hexane/ethyl acetate = 20/1 to afford *N*-phenylhexylamine a colorless oil (152 mg, 86% isolated yield).

15 Example 89

Procedure for amination of bromobenzene under an air atmosphere

Copper (I) iodide (10 mg, 0.05 mmol, 5 mol%), anhydrous fine powder potassium phosphate (425 mg, 2.0 mmol) and 2-phenylphenol (34 mg, 0.2 mmol, 20 mol%) were put into a screw-capped test tube with a Teflon septum. Anhydrous toluene (1.0 mL), 20 bromobenzene (105 µL, 1.0 mmol) and *n*-hexylamine (158 µL, 1.2 mmol) were added by micro-syringe at room temperature under air atmosphere. The reaction mixture was heated at 100 °C for 22 hours. The reaction mixture was then allowed to reach room temperature. Diethyl ether (2 mL), water (2 mL) and dodecane (internal standard, 227 µL) were added. The organic layer was analyzed by GC to give 33% GC yield of *N*-phenylhexylamine.

30 Example 90

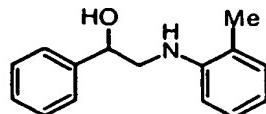
Procedures for amination of aryl iodides in toluene under an argon atmosphere

Iodobenzene substrate

Copper (I) iodide (10 mg, 0.05 mmol, 5 mol%), anhydrous fine powder potassium phosphate (425 mg, 2.0 mmol) and 2,6-dimethylphenol (24 mg, 0.2 mmol, 20 mol%) were put into a screw-capped test tube with a Teflon septum. The tube was evacuated and back-filled with argon (3 cycles). Iodobenzene (112 μ L, 1.0 mmol) and *n*-hexylamine (158 μ L, 1.0 mmol) were added by micro-syringe at room temperature. The reaction mixture was heated at 80 °C for 18 hours. The reaction mixture was then allowed to reach room temperature. Diethyl ether (2 mL), water (2 mL) and dodecane (internal standard, 227 μ L) were added. The organic layer was analyzed by GC to give 41% GC yield of *N*-phenylhexylamine.

2-Iodoanisole substrate

Copper (I) iodide (10 mg, 0.05 mmol, 5 mol%), anhydrous fine powder potassium phosphate (425 mg, 2.0 mmol) and 2,6-dimethylphenol (24 mg, 0.2 mmol, 20 mol%) were put into a screw-capped test tube with a Teflon septum. The tube was evacuated and back-filled with argon (3 cycles). 2-Iodoanisole (130 μ L, 1.0 mmol) and *n*-hexylamine (158 μ L, 1.0 mmol) were added by micro-syringe at room temperature. The reaction mixture was heated at 80 °C for 18 hours. The reaction mixture was then allowed to reach room temperature. Diethyl ether (2 mL), water (2 mL) and dodecane (internal standard, 227 μ L) were added. The organic layer was analyzed by GC to give 41% GC yield of *N*-(2-methoxyphenyl)hexylamine.

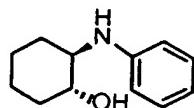
*Example 91*1-Phenyl-2-(2-tolylamino)ethanol

A 15 mL screw top test tube fitted with a PTFE septum cap was purged with argon before addition of CuI (5.0 mg, 0.026 mmol, 2.6 mol%), NaOH (83.0 mg, 2.08 mmol), and *rac*-2-amino-1-phenylethanol (143 mg, 1.04 mmol). 2-Iodotoluene (159 μ L, 1.25 mmol) and isopropyl alcohol (1.0 mL) were added, via syringe, under argon. The septum cap was replaced with a solid, Teflon-lined cap and the reaction was stirred magnetically at 90 °C for 48 h. The resulting homogeneous solution was allowed to cool before dilution with 10 mL brine. The reaction mixture was transferred to a separatory funnel and extracted with

methylene chloride (3×10 mL). The organics were washed with 0.1 M NaOH (2×10 mL), washed with brine (1×15 mL), dried over MgSO₄ and concentrated. The crude material was purified by silica gel chromatography using methylene chloride. The product was obtained as a pale yellow, viscous oil in 92% yield (217.4 mg).

5 *Example 92*

trans-2-Phenylamino cyclohexanol

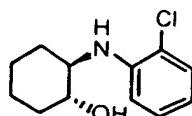


A 15 mL screw top test tube fitted with a PTFE septum cap was purged with argon before addition of CuI (5.0 mg, 0.026 mmol, 2.6 mol%), NaOH (83.0 mg, 2.08 mmol) and 10 *rac*-2-amino-1-cyclohexanol HCl (158 mg, 1.04 mmol). Iodobenzene (139 μ L, 1.25 mmol), dimethyl sulfoxide (670 μ L), and a stock solution of 9.45 M NaOH (330 μ L, 3.12 mmol) were added, via syringe, under argon. The septum cap was replaced with a solid, Teflon-lined cap and the reaction was stirred magnetically at 90 °C for 48 h. The resulting homogeneous solution was allowed to cool before dilution with 10 mL brine. The reaction mixture was transferred to a separatory funnel and extracted with diethyl ether (3×10 mL). The organic extracts were washed with 3 M HCl (3×10 mL). The acid extracts were then cooled in an ice bath and the solution was basified using a saturated NaOH solution. When the pH of the solution became basic, as indicated by pH paper, the solution became opaque. The mixture was transferred to a separatory funnel and extracted with methylene chloride. 15 (3×10 mL). The organic extract was washed with brine, dried over MgSO₄ and concentrated. A pale yellow oil was obtained and placed under high vacuum overnight. While under vacuum the oil solidified to give 182.5 mg (92% yield) of an off-white solid, mp 57-58 °C.

20

Example 93

25 *trans*-2-(2-Chlorophenylamino) cyclohexanol

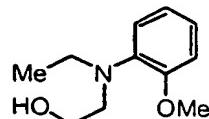


A 15 mL screw top test tube fitted with a PTFE septum cap was purged with argon before addition of CuI (5.0 mg, 0.026 mmol, 2.6 mol%), NaOH (125 mg, 3.12 mmol) and

rac-2-amino-1-cyclohexanol HCl (158 mg, 1.04 mmol), 2-Chloro-1-iodobenzene (152 μ L, 1.25 mmol) and isopropyl alcohol (1.0 mL) were added, via syringe, under argon. The septum cap was replaced with a solid, Teflon-lined cap and the reaction was stirred magnetically at 90 °C for 48 h. The resulting homogeneous solution was allowed to cool before dilution with 10 mL brine. The reaction mixture was transferred to a separatory funnel and extracted with methylene chloride (3 x 10 mL). The organics were washed with brine, dried over MgSO₄ and concentrated. The crude material was purified by silica gel chromatography using hexanes / ethyl acetate (60:40). The product was obtained as a yellow oil in 91% yield (212.7 mg).

10 Example 94

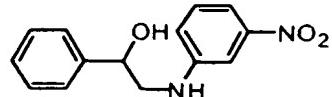
2-[Ethyl-(2-methoxyphenyl)amino] ethanol



A 15 mL screw top test tube fitted with a PTFE septum cap was purged with argon before addition of CuI (5.0 mg, 0.026 mmol, 2.6 mol%) and NaOH (83.0 mg, 2.08 mmol). 15 2-(aminoethyl)-ethanol (101 μ L, 1.04 mmol), 2-iodoanisole (162 μ L, 1.25 mmol) and isopropyl alcohol (1.0 mL) were added, via syringe, under argon. The septum cap was replaced with a solid, Teflon-lined cap and the reaction was stirred magnetically at 90 °C for 48 h. The resulting homogeneous solution was allowed to cool before dilution with 10 mL brine. The reaction mixture was transferred to a separatory funnel and extracted with 20 methylene chloride (3 x 10 mL). The organics were washed with 0.1 M NaOH (2 x 10 mL), washed with brine (1 x 15 mL), dried over MgSO₄ and concentrated. The crude material was purified by silica gel chromatography using methylene chloride/ethyl acetate (70:30). The product was obtained as a pale yellow, viscous oil in 72% yield (145.8 mg).

25 Example 95

2-(3-Nitrophenylamino)-1-phenylethanol

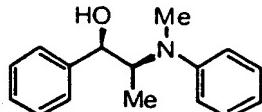


A 15 mL screw top test tube fitted with a PTFE septum cap was purged with argon before addition of CuI (5.0 mg, 0.026 mmol, 2.6 mol%), K₃PO₄ (425 mg, 2.0 mmol), *rac*-2-

amino-1-phenylethanol (140 mg, 1.02 mmol) and 1-iodo-3-nitrobenzene (302 mg, 1.25 mmol). Ethylene glycol (56 μ L, 1.02 mmol) and isopropyl alcohol (1.0 mL) were added, via syringe, under argon. The septum cap was replaced with a solid, Teflon-lined cap and the reaction was stirred magnetically at 75 °C for 48 h. The reaction mixture was allowed 5 to cool before dilution with 10 mL brine and extraction with methylene chloride (3 x 10 mL). The organic extracts were washed with 0.1 M NaOH (2 x 10 mL), washed with brine (1 x 15 mL), dried over MgSO₄ and concentrated. The crude material was purified by silica gel chromatography using methylene chloride / ethyl acetate (96:4). The product was obtained as an orange, viscous oil in 66% yield (172.8 mg).

10 **Example 96**

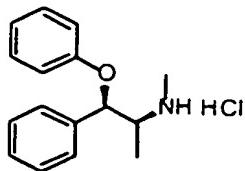
N-Phenylephedrine



A 15 mL screw top test tube fitted with a PTFE septum cap was purged with argon before addition of CuI (10.0 mg, 0.052 mmol, 5.2 mol%), NaOtBu (288 mg, 3.0 mmol) and 15 (*1R, 2S*)-ephedrine HCl (202 mg, 1.0 mmol). Iodobenzene (168 μ L, 1.5 mmol) and dimethyl sulfoxide (1.25 mL) were added, via syringe, under argon. The septum cap was replaced with a solid, Teflon-lined cap and the reaction was stirred magnetically at 100 °C for 22 h. The resulting solution was allowed to cool before dilution with 10 mL brine. The reaction mixture was transferred to a separatory funnel and extracted with methylene 20 chloride (3 x 10 mL). The organics were washed with 0.1 M NaOH (2 x 10 mL), washed with brine (1 x 15 mL), dried over MgSO₄ and concentrated. The crude material was purified by silica gel chromatography using methylene chloride. The product was obtained as a pale yellow, viscous oil in 72% yield (175 mg). ¹H NMR (500 MHz, CDCl₃): 1.16 (d, J = 6.9 Hz, 3H), 2.39 (broad s, 1H), 2.70 (s, 3H), 4.01 (dq, J = 6.9, 5.5 Hz, 1H), 25 ~ 4.74 (d, J = 5.2 Hz, 1H), 6.68 (m, 3H), 7.20 (m, 7H). ¹³C NMR (125 MHz, CDCl₃): 12.1, 32.4, 59.5, 75.9, 113.3, 116.8, 125.9, 127.3, 128.1, 129.0, 142.5, 150.0.

Example 97

Preparation of O-phenylephedrine



A 15 mL screw top test tube fitted with a PTFE septum cap was charged with CuI (10.0 mg, 0.05 mmol, 5 mol%), Cs₂CO₃ (652 mg, 2.00 mmol), and (1*R*,2*S*)-ephedrine (165 mg, 1.00 mmol). Iodobenzene (168 μ L, 1.50 mmol) and butyronitrile (1 mL) were added, 5 via syringe, while purging with nitrogen. The septum cap was replaced with a solid, Teflon-lined cap and the reaction was stirred magnetically at 125 °C for 25.5 h. The resulting heterogeneous solution was allowed to cool before dilution with 5 mL ethyl acetate. The reaction mixture was filtered and the solvent was removed to yield a dark oil; this oil was taken up in a small volume of ether and then added to dilute HCl. The resulting 10 white precipitate was collected by vacuum filtration and washed well with hexanes. After drying in vacuo, a 67 % yield (187.1 mg) of the HCl salt was obtained. All characterization data are for the free base. ¹H NMR (300 MHz, CDCl₃): δ 1.12 (d, *J* = 6.3 Hz, 3H), 1.34 (broad s, 1H), 2.43 (s, 3H), 2.92 (dq, *J* = 6.6, 4.4 Hz, 1H), 5.17 (d, 1H), 6.83 (m, 3H), 7.22 (m, 7H). ¹³C NMR (75.5 MHz, CDCl₃): 14.8, 34.0, 60.3, 81.3, 115.6, 120.6, 126.4, 127.4, 128.3, 129.1, 139.2, 158.0.

Example 98

Benzyl phenylamine using sodium hydroxide as base in DMSO

A 15 mL screw top test tube fitted with a PTFE septum cap was purged with argon before addition of CuI (10.0 mg, 0.052 mmol, 5 mol%). Iodobenzene (116 μ L, 1.04 mmol), 20 benzylamine (114 μ L, 1.04 mmol), dimethylsulfoxide (660 μ L) and 6.33 M NaOH (330 μ L, 2.08 mmol) were added via syringe. The test tube was purged with argon before replacing the septum cap with a solid, Teflon-lined cap. The reaction was stirred magnetically at 110 °C for 4.25 h. The reaction mixture was allowed to cool before dilution with 10 mL water and extraction with diethyl ether (3 x 10 mL). The organic extracts were washed with 3.0 25 M HCl (3 x 10 mL). The acid extracts were cooled in an ice bath and the solution was basified using a saturated NaOH solution. When the pH of the solution became basic, as indicated by pH paper, the solution became opaque. The mixture was transferred to a separatory funnel and extracted with methylene chloride (3 x 10 mL). The organic extract

was washed with brine, dried over MgSO₄ and concentrated. The product was obtained as a pale yellow, viscous oil in 19% yield (35.9 mg).

Example 99

- 5 N-Phenylbenzylamine, N-phenyl-N-methylbenzylamine, N-phenyl-(1-phenylethyl)amine, and N-phenylpiperidine using sodium hydroxide as base in DMSO

A 15 mL screw top test tube fitted with a PTFE septum cap was purged with argon before addition of CuI (10.0 mg, 0.052 mmol, 5 mol%). Iodobenzene (116 µL, 1.04 mmol), amine (1.04 mmol), dimethylsulfoxide (660 µL) and 6.33 M NaOH (330 µL, 2.08 mmol) were added via syringe. The test tube was purged with argon before replacing the septum cap with a solid, Teflon-lined cap. The reaction was stirred magnetically at 95 °C for 20.5 h. The reaction mixture was allowed to cool before dilution with 5 mL water and 5 mL diethyl ether. An aliquot was removed for GC analysis; GC yields were 26%, 6%, 12%, and 13%, respectively.

Example 100

- 15 N-Arylation of 5-amino-1-pentanol and 4-amino-1-butanol using sodium hydroxide as base in DMSO

A 15 mL screw top test tube fitted with a PTFE septum cap was purged with argon before addition of CuI (10.0 mg, 0.052 mmol, 5 mol%). Iodobenzene (116 µL, 1.04 mmol), aminoalcohol (1.04 mmol), dimethylsulfoxide (660 µL) and 6.33 M NaOH (330 µL, 2.08 mmol) were added via syringe. The test tube was purged with argon before replacing the septum cap with a solid, Teflon-lined cap.. The reaction was stirred magnetically at 90 °C for 24 h. The reaction mixture was allowed to cool before dilution with 10 mL water and extraction with diethyl ether (3 x 10 mL). The organic extracts were washed with 3.0 M HCl (3 x 10 mL). The acid extracts were cooled in an ice bath and the solution was basified using a saturated NaOH solution. When the pH of the solution became basic, as indicated by pH paper, the solution became opaque. The mixture was transferred to a separatory funnel and extracted with methylene chloride (3 x 10 mL). The organic extract was washed with brine, dried over MgSO₄ and concentrated. A pale yellow oil was obtained and placed under high vacuum overnight. The products were obtained as light yellow, viscous oils; the isolated yields were 49% and 47%, respectively.

Example 101

- 2-Phenylamino ethanol using sodium hydride as base in THF

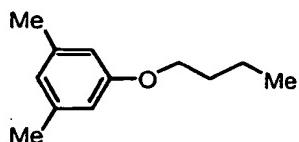
An oven-dried 15 mL screw top test tube fitted with a PTFE septum cap was purged with argon before addition of CuI (10.0 mg, 0.052 mmol, 5 mol%), NaH (60 % dispersion in mineral oil, 25 mg, 1.04 mmol), ethanolamine (63 μ L, 1.04 mmol) and tetrahydrofuran (1 mL). The reaction was stirred until bubbling subsided. Iodobenzene (116 μ L, 1.04 mmol)

5 was added via syringe and the test tube was purged with argon before replacing the septum cap with a solid, Teflon-lined cap. The reaction was stirred magnetically at 65 °C for 24 h. The reaction mixture was allowed to cool before dilution with 10 mL water and extraction with diethyl ether (3 x 10 mL). The organic extracts were washed with brine, dried over MgSO₄ and concentrated. The crude material was purified by column chromatography

10 using hexane/ethyl acetate (25:75). The product was obtained as an oil in 52% yield. ¹H NMR (500 MHz, CDCl₃): 2.54 (broad s, 1H), 3.24 (t, J = 5.2 Hz, 2H), 3.76 (t, J = 5.2 Hz, 2H), 4.00 (broad s, 1H), 6.62 (m, 2H), 6.73 (m, 1H), 7.17 (m, 2H). ¹³C NMR (125 MHz, CDCl₃): 46.0, 61.0, 113.2, 117.8, 129.2, 148.0.

Example 102

15 **Preparation of 1-butoxy-3,5-dimethylbenzene without solvent using 2-phenylphenol as ligand and cesium carbonate as base**



A screw cap test tube was charged with *n*-butanol (1.37 mL, 15.0 mmol), 3,5-dimethyliodobenzene (150 μ L, 1.04 mmol), CuI (19.8 mg, 0.104 mmol), Cs₂CO₃ (977 mg, 20 3.00 mmol) and 2-phenylphenol (88.5 mg, 0.520 mmol). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 105 °C for 40 hours. The reaction mixture was allowed to reach room temperature. Dodecane (237 μ L, 1.04 mmol; internal standard) was added and a GC sample was filtered through Celite and eluted with CH₂Cl₂. GC analysis revealed 64% yield of the desired product. The identity of the product was confirmed by ¹H NMR and GC-MS (signal at 178 m/z). ¹H NMR (400 MHz, CDCl₃): δ 6.52 (s, 1H), 6.47 (s, 2H), 3.88 (t, J = 6.5 Hz, 2H), 2.21 (s, 6H), 1.72-1.63 (m, 2H), 1.47-1.32 (m, 2H), 0.90 (t, J = 7.4 Hz, 3H).

Example 103**Preparation of 1-butoxy-3,5-dimethylbenzene without solvent using 2-phenylphenol as ligand and potassium phosphate as base**

A screw cap test tube was charged with *n*-butanol (1.37 mL, 15.0 mmol), 3,5-dimethyliodobenzene (150 μ L, 1.04 mmol), CuI (19.8 mg, 0.104 mmol), K_3PO_4 (571 mg, 2.69 mmol) and 2-phenylphenol (88.5 mg, 0.520 mmol). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 105 °C for 40 hours. The reaction mixture was allowed to reach room temperature. Dodecane (237 μ L, 1.04 mmol; internal standard) was added and a GC sample was filtered through Celite and eluted with CH_2Cl_2 . GC analysis revealed 5% yield of the desired product.

Example 104**Preparation of 1-butoxy-3,5-dimethylbenzene using various ligands**

A screw cap test tube was charged with *n*-butanol (573 μ L, 6.26 mmol), 3,5-dimethyliodobenzene (144 μ L, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), Cs_2CO_3 (977 mg, 3.00 mmol), the ligand (0.500 mmol) and toluene (1 mL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 105 °C for 36 hours. The reaction mixture was allowed to reach room temperature. Dodecane (227 μ L, 1.00 mmol; internal standard) was added and a GC sample was filtered through Celite and eluted with CH_2Cl_2 . The yield of the desired product was determined using GC analysis; the results are tabulated below.

Ligand	GC yield
2-Phenylphenol	81%
2,6-Dimethylphenol	75%
2-Isopropylphenol	65%
1-Naphthol	43%
2-(Dimethylamino)ethanol	46%
<i>N,N</i> -Dimethylglycine	73%
Methyliminodiacetic acid	28%
<i>N,N,N',N'</i> -Tetramethylethylenediamine	20%

Example 105

Preparation of 1-butoxy-3,5-dimethylbenzene using various solvents

A screw cap test tube was charged with *n*-butanol (573 μ L, 6.26 mmol), 3,5-dimethyliodobenzene (144 μ L, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), Cs₂CO₃ (977 mg, 3.00 mmol), 2-phenylphenol (85.1 mg, 0.500 mmol) and the solvent (1 mL). The test tube
5 was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 90 °C for 36 hours. The reaction mixture was allowed to reach room temperature. Dodecane (227 μ L, 1.00 mmol; internal standard) was added and a GC sample was filtered through Celite and eluted with CH₂Cl₂. The yield of the desired product was determined using GC analysis; the results are tabulated below.

Solvent	GC yield
1,4-Dioxane	46%
1,2-Dimethoxyethane	42%
Triethylamine	55%

10

Example 106

Preparation of 1-butoxy-3,5-dimethylbenzene without ligand using cesium carbonate as base and toluene as solvent

A screw cap test tube was charged with *n*-butanol (1.25 mL, 13.7 mmol), 3,5-dimethyliodobenzene (144 μ L, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), Cs₂CO₃ (977 mg, 3.00 mmol) and toluene (1 mL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 105 °C for 42 hours. The reaction mixture was allowed to reach room temperature. Dodecane (227 μ L, 1.00 mmol; internal standard) was added and a GC sample was filtered through Celite and eluted with CH₂Cl₂. GC analysis revealed 50% yield of the desired product.
20

Example 107

Preparation of 1-butoxy-3,5-dimethylbenzene using 1,10-phenanthroline as ligand, cesium carbonate as base and toluene as solvent

A screw cap test tube was charged with *n*-butanol (183 μ L, 2.00 mmol), 3,5-dimethyliodobenzene (144 μ L, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), Cs₂CO₃ (977 mg, 3.00 mmol), 1,10-phenanthroline (90.1 mg, 0.500 mmol) and toluene (1 mL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at

110 °C for 40 hours. The reaction mixture was allowed to reach room temperature. Dodecane (227 µL, 1.00 mmol; internal standard) was added and a GC sample was filtered through Celite and eluted with CH₂Cl₂. GC analysis revealed 83% yield of the desired product.

5 **Example 108**

4-Butoxyaniline

A test tube was charged with CuI (20 mg, 0.10 mmol, 10 mol%), 1,10-phenanthroline (36 mg, 0.20 mmol, 20 mol%), Cs₂CO₃ (456 mg, 1.4 mmol), 4-iodoaniline (219 mg, 1.0 mmol) and *n*-butanol (1.0 mL). The test tube was sealed and the reaction mixture was stirred at 110 °C for 23 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with ethyl acetate. The filtrate was concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; hexane/ethyl acetate 10:1) provided 66 mg (40% yield) of the title compound as a red-brown oil.

15 **Example 109**

2-Butoxytoluene

A test tube was charged with CuI (20 mg, 0.10 mmol, 10 mol%), 1,10-phenanthroline (36 mg, 0.20 mmol, 20 mol%), Cs₂CO₃ (456 mg, 1.4 mmol), 2-iodotoluene (127 µL, 1.0 mmol) and *n*-butanol (1.0 mL). The test tube was sealed and the reaction mixture was stirred at 110 °C for 23 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with ethyl acetate. The filtrate was concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; hexane) provided 159 mg (97% yield) of the title compound as a colorless oil.

Example 110

25 **Preparation of 3-butoxyanisole using 5 mol% CuI**

A test tube was charged with CuI (10 mg, 0.050 mmol, 5 mol%), 1,10-phenanthroline (36 mg, 0.20 mmol, 20 mol%), Cs₂CO₃ (456 mg, 1.4 mmol), 3-iodoanisole (119 µL, 1.0 mmol) and *n*-butanol (1.0 mL). The test tube was sealed and the reaction mixture was stirred at 110 °C for 20 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with ethyl acetate. The

mL). The test tube was sealed and the reaction mixture was stirred at 110 °C for 32 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with ethyl acetate. The filtrate was concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; hexane/ethyl acetate 30:1) provided 173 mg (76% yield, 98% ee) of the title compound as a colorless oil.

Example 120

Preparation of 1-heptoxy-3,5-dimethylbenzene using low catalyst loading

A screw cap test tube was charged with *n*-heptanol (283 µL, 2.00 mmol), 3,5-dimethyliodobenzene (144 µL, 1.00 mmol), CuI (4.75 mg, 0.025 mmol), 1,10-phenanthroline (1.80 mg, 0.01 mmol), Cs₂CO₃ (977 mg, 3.00 mmol) and *o*-xylene (1 mL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 120 °C for 19 hours. The reaction mixture was allowed to reach room temperature. Dodecane (227 µL, 1.00 mmol; internal standard) was added and a GC sample was filtered through Celite and eluted with CH₂Cl₂. GC analysis revealed 64% yield of the desired product.

Example 121

General procedure for the preparation of 1-heptoxy-3,5-dimethylbenzene using various solvents

A screw cap test tube was charged with *n*-heptanol (283 µL, 2.00 mmol), 3,5-dimethyliodobenzene (144 µL, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), 1,10-phenanthroline (90.1 mg, 0.500 mmol), Cs₂CO₃ (977 mg, 3.00 mmol) and solvent (1 mL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 120 °C for 40 hours. The reaction mixture was allowed to reach room temperature. Dodecane (227 µL, 1.00 mmol; internal standard) was added and a GC sample was filtered through Celite and eluted with CH₂Cl₂. The yield of the desired product was determined using GC analysis; the results are tabulated below.

Solvent	GC yield
DMF	52%
tri- <i>n</i> -propylamine	40%
<i>n</i> -butyronitrile	62%
DMSO	41%

by flash chromatography on silica gel (2×20 cm; hexane/ethyl acetate 30:1) provided 152 mg (87% yield) of the title compound as a colorless oil.

Example 117

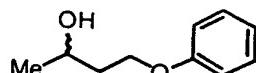
3-Methoxybenzonitrile

5 A test tube was charged with CuI (20 mg, 0.10 mmol, 10 mol%), 1,10-phenanthroline (36 mg, 0.20 mmol, 20 mol%), Cs₂CO₃ (652 mg, 2.0 mmol), 3-iodobenzonitrile (229 mg, 1.0 mmol), methanol (162 µL, 4.0 mmol) and toluene (1 mL). The test tube was sealed and the reaction mixture was stirred at 110 °C for 23 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of 10 silica gel eluting with diethyl ether. The filtrate was concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane/diethyl ether 5:1) provided 111 mg (84% yield) of the title compound as a colorless oil.

Example 118

Regioselective preparation of 4-phenoxy-2-butanol from 1,3-butanediol

15

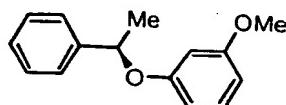


20

A screw cap test tube was charged with 1,3-butanediol (178 µL, 2.00 mmol), iodobenzene (112 µL, 1.00 mmol), CuI (19.4 mg, 0.100 mmol), 5-methyl-1,10-phenanthroline (38.8 mg, 0.200 mmol), Cs₂CO₃ (652 mg, 2.00 mmol) and toluene (1.0 mL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 110 °C for 44 hours. The reaction mixture was allowed to reach room temperature. The reaction mixture was filtered over a short silica gel plug eluting with CH₂Cl₂. The solvent was removed under reduced pressure. Chromatography on silica gel (35 g, pentane/EtOAc 5:1) afforded the desired product in 55 % yield.

Example 119

25 (R)-3-(1-phenylethoxy)anisole



A test tube was charged with CuI (20 mg, 0.10 mmol, 10 mol%), 5-methyl-1,10-phenanthroline (39 mg, 0.20 mmol, 20 mol%), Cs₂CO₃ (652 mg, 2.0 mmol), 3-iodoanisole (119 µL, 1.0 mmol), (R)-(+)-1-phenylethanol (205 µL, 1.7 mmol, >99% ee) and toluene (1

(2×20 cm; pentane/diethyl ether 30:1) provided 128 mg (67% yield) of the title compound as a colorless oil.

Example 114

3-Ethoxyanisole

5 A test tube was charged with CuI (20 mg, 0.10 mmol, 10 mol%), 1,10-phenanthroline (36 mg, 0.20 mmol, 20 mol%), Cs₂CO₃ (456 mg, 1.4 mmol), 3-iodoanisole (119 µL, 1.0 mmol) and ethanol (1.0 mL). The test tube was sealed and the reaction mixture was stirred at 110 °C for 20 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with diethyl ether. The filtrate was
10 concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane/diethyl ether 30:1) provided 142 mg (93% yield) of the title compound as a colorless oil.

Example 115

2-Methoxybenzyl alcohol

15 A test tube was charged with CuI (20 mg, 0.10 mmol, 10 mol%), 1,10-phenanthroline (36 mg, 0.20 mmol, 20 mol%), Cs₂CO₃ (456 mg, 1.4 mmol), 2-iodobenzylalcohol (234 mg, 1.0 mmol) and methanol (1.0 mL). The test tube was sealed and the reaction mixture was stirred at 80 °C for 24 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with diethyl
20 ether. The filtrate was concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane/diethyl ether 2:1) provided 122 mg (88% yield) of the title compound as a colorless oil.

Example 116

3-Butoxybenzonitrile

25 A test tube was charged with CuI (20 mg, 0.10 mmol, 10 mol%), 5-methyl-1,10-phenanthroline (39 mg, 0.20 mmol, 20 mol%), Cs₂CO₃ (652 mg, 2.0 mmol), 3-iodobenzonitrile (229 mg, 1.0 mmol), *n*-butanol (366 µL, 4.0 mmol) and toluene (1 mL). The test tube was sealed and the reaction mixture was stirred at 110 °C for 28 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of
30 silica gel eluting with ethyl acetate. The filtrate was concentrated. Purification of the residue

filtrate was concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; hexane) provided 177 mg (98% yield) of the title compound as a pale yellow oil.

Example 111

3-Butoxypyridine

- 5 A test tube was charged with CuI (20 mg, 0.10 mmol, 10 mol%), 1,10-phenanthroline (36 mg, 0.20 mmol, 20 mol%), Cs₂CO₃ (652 mg, 2.0 mmol), 3-iodopyridine (205 mg, 1.0 mmol) and *n*-butanol (1.0 mL). The test tube was sealed and the reaction mixture was stirred at 110 °C for 23 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with ethyl acetate. The
10 filtrate was concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; hexane/ethyl acetate 8:1) provided 125 mg (83% yield) of the title compound as a light yellow oil.

Example 112

4-Isopropoxyanisole

- 15 A test tube was charged with CuI (20 mg, 0.10 mmol, 10 mol%), 1,10-phenanthroline (36 mg, 0.20 mmol, 20 mol%), Cs₂CO₃ (456 mg, 1.4 mmol), 4-iodoanisole (234 mg, 1.0 mmol) and isopropanol (1.0 mL). The test tube was sealed and the reaction mixture was stirred at 110 °C for 23 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with ethyl acetate. The
20 filtrate was concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; hexane/ethyl acetate 20:1) provided 138 mg (83% yield) of the title compound as a colorless oil.

Example 113

4-Cyclopentoxyanisole

- 25 A test tube was charged with CuI (20 mg, 0.10 mmol, 10 mol%), 5-methyl-1,10-phenanthroline (39 mg, 0.20 mmol, 20 mol%), Cs₂CO₃ (652 mg, 2.0 mmol), 4-iodoanisole (234 mg, 1.0 mmol) and cyclopentanol (1.0 mL). The test tube was sealed and the reaction mixture was stirred at 110 °C for 24 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with diethyl ether. The
30 filtrate was concentrated. Purification of the residue by flash chromatography on silica gel

Example 122**General procedure for the preparation of 1-heptoxy-3,5-dimethylbenzene using various nitrogen ligands**

5 A screw cap test tube was charged with *n*-heptanol (283 µL, 2.00 mmol), 3,5-dimethyliodobenzene (144 µL, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), ligand (0.200 mmol), Cs₂CO₃ (977 mg, 3.00 mmol) and *o*-xylene (1 mL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 120 °C for 19 hours. The reaction mixture was allowed to reach room temperature. Dodecane (227 µL, 1.00 mmol; internal standard) was added and a GC sample was filtered through Celite and eluted with CH₂Cl₂. The yield of the desired product was determined using GC analysis; the results are tabulated below.

Ligand	GC yield
8-Hydroxyquinoline	30%
2-(Aminomethyl)pyridine	28%
8-Aminoquinoline	6%

Example 123**Preparation of 1-heptoxy-3,5-dimethylbenzene using *trans*-N,N'-dimethyl-1,2-diaminocyclohexane as ligand**

15 A screw cap test tube was charged with *n*-heptanol (283 µL, 2.00 mmol), 3,5-dimethyliodobenzene (144 µL, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), *trans*-N,N'-dimethyl-1,2-diaminocyclohexane (71.1 mg, 0.500 mmol), Cs₂CO₃ (977 mg, 3.00 mmol) and *o*-xylene (1 mL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 140 °C for 17 hours. The reaction mixture was allowed to reach room temperature. Dodecane (227 µL, 1.00 mmol; internal standard) was added and a GC sample was filtered through Celite and eluted with CH₂Cl₂. GC analysis revealed 67% yield of the desired product.

Example 124**General procedure for the preparation of 1-heptoxy-3,5-dimethylbenzene using various 1,10-phenanthroline type ligands**

A screw cap test tube was charged with *n*-heptanol (283 µL, 2.00 mmol), 3,5-dimethyliodobenzene (144 µL, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), ligand (0.200 mmol), Cs₂CO₃ (977 mg, 3.00 mmol) and toluene (1 mL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 110 °C for 39 hours. The reaction mixture was allowed to reach room temperature. Dodecane (227 µL, 1.00 mmol; internal standard) was added and a GC sample was filtered through Celite and eluted with CH₂Cl₂. The yield of the desired product was determined using GC analysis; the results are tabulated below.

Ligand	GC yield
1,10-Phenanthroline	81%
4,7-Diphenyl-1,10-phenanthroline	91%
4,7-Dimethyl-1,10-phenanthroline	85%
5-Methyl-1,10-phenanthroline	95%
5-Chloro-1,10-phenanthroline	90%
5-Nitro-1,10-phenanthroline	41%

Example 125**Preparation of 1-heptoxy-3,5-dimethylbenzene at 70 °C**

A screw cap test tube was charged with *n*-heptanol (283 µL, 2.00 mmol), 3,5-dimethyliodobenzene (144 µL, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), 5-methyl-1,10-phenanthroline (38.8 mg, 0.200 mmol), Cs₂CO₃ (977 mg, 3.00 mmol) and toluene (0.5 mL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 70 °C for 23 hours. The reaction mixture was allowed to reach room temperature. Dodecane (227 µL, 1.00 mmol; internal standard) was added and a GC sample was filtered through Celite and eluted with CH₂Cl₂. GC analysis revealed 68 % yield of the desired product.

Example 126**Preparation of 1-heptoxy-3,5-dimethylbenzene at 70 °C in *n*-heptanol as solvent**

A screw cap test tube was charged with *n*-heptanol (1.00 mL), 3,5-dimethyliodobenzene (144 µL, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), 5-methyl-1,10-phenanthroline (38.8 mg, 0.200 mmol) and Cs₂CO₃ (977 mg, 3.00 mmol). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 70 °C 5 for 48 hours. The reaction mixture was allowed to reach room temperature. Dodecane (227 µL, 1.00 mmol; internal standard) was added and a GC sample was filtered through Celite eluting with CH₂Cl₂. GC analysis revealed 100 % yield of the desired product.

Example 127

Preparation of 1-heptoxy-3,5-dimethylbenzene at room temperature in *n*-heptanol as solvent

10 A screw cap test tube was charged with *n*-heptanol (1.00 mL), 3,5-dimethyliodobenzene (144 µL, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), 5-methyl-1,10-phenanthroline (38.8 mg, 0.200 mmol) and Cs₂CO₃ (977 mg, 3.00 mmol). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically at room temperature for 29 hours. Dodecane (227 µL, 1.00 mmol; internal standard) was added and a GC sample 15 was filtered through Celite eluting with CH₂Cl₂. GC analysis revealed 18% yield of the desired product.

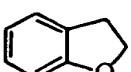
Example 128

Preparation of 1-heptoxy-3,5-dimethylbenzene from 3,5-dimethylbromobenzene

20 A screw cap test tube was charged with *n*-heptanol (283 µL, 2.00 mmol), 3,5-dimethylbromobenzene (136 µL, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), 1,10-phenanthroline (90.1 mg, 0.500 mmol), Cs₂CO₃ (977 mg, 3.00 mmol) and *o*-xylene (1 mL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 140 °C for 44 hours. The reaction mixture was allowed to reach room 25 temperature. Dodecane (227 µL, 1.00 mmol; internal standard) was added and a GC sample was filtered through Celite and eluted with CH₂Cl₂. GC analysis revealed 16% yield of the desired product.

Example 129

Preparation of 2,3-dihydrobenzofuran from 2-bromophenethyl alcohol using 5-methyl-1,10-phenanthroline as the ligand

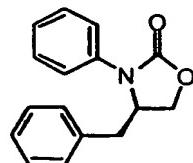


30

A screw cap test tube was charged with 2-bromophenethyl alcohol (136 μ L, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), 5-methyl-1,10-phenanthroline (38.8 mg, 0.200 mmol), Cs₂CO₃ (977 mg, 3.00 mmol) and toluene (1 mL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 110 °C for 43 hours. The 5 reaction mixture was allowed to reach room temperature. Dodecane (227 μ L, 1.00 mmol; internal standard) was added and a GC sample was filtered through Celite and eluted with CH₂Cl₂. GC analysis revealed 72% yield of the desired product.

Example 130

(R)-4-Benzyl-3-phenyl-2-oxazolidinone

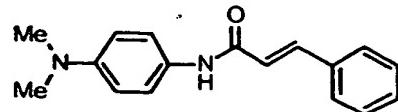


10

A 15 mL resealable Schlenk tube was charged with CuI (9.6 mg, 0.0504 mmol, 5.0 mol%), (R)-4-benzyl-2-oxazolidinone (215 mg, 1.21 mmol), K₂CO₃ (280 mg, 2.03 mmol), evacuated and backfilled with argon. Racemic *trans*-*N,N'*-dimethyl-1,2-cyclohexanediamine (16 μ L, 0.102 mmol, 10 mol%), iodobenzene (106 μ L, 0.947 mmol) 15 and toluene (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 80 °C for 24 h. The resulting pale blue suspension was allowed to reach room temperature and then filtered through a 0.5×1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2×15 cm, hexane-ethyl acetate 20 2:1, 15 mL fractions). Fractions 11-19 provided 238 mg (99% yield) of the desired product as a pale tan solid. HPLC analysis on a Daicel OD column (hexane-isopropanol 85:15, 0.7 mL/min, t₁(R) = 23.3 min, t₁(S) = 26.7 min) indicated >99.5% ee.

Example 131

***trans*-N-(4-Dimethylaminophenyl)-3-phenylpropenamide**



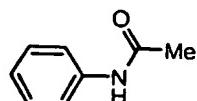
25

A 15 mL resealable Schlenk tube was charged with CuI (9.6 mg, 0.0504 mmol, 5.0 mol%), 4-dimethylamino-1-bromobenzene (201 mg, 1.00 mmol), *trans*-cinnamamide (178

mg, 1.21 mmol), K_2CO_3 (280 mg, 2.03 mmol), evacuated and backfilled with argon. *trans*-*N,N'*-Dimethyl-1,2-cyclohexanediamine (16 μ L, 0.102 mmol, 10 mol%) and toluene (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 110 °C for 23 h. The resulting bright yellow suspension was
 5 allowed to reach room temperature and then filtered through a 0.5x1 cm pad of silica gel eluting with 10 mL of ethyl acetate-dichloromethane 1:1. The filtrate was concentrated, the residue was dissolved in 10 mL of dichloromethane and purified by flash chromatography on silica gel (2x20 cm, ethyl acetate-dichloromethane 1:4, 15 mL fractions). Fractions 10-20 provided 261 mg (98% yield) of the desired product as a bright yellow solid.

10 Example 132

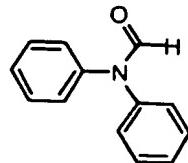
Preparation of *N*-phenylacetamide at 60 °C for 4 h



A 15 mL resealable Schlenk tube was charged with CuI (10 mg, 0.0525 mmol, 5.0 mol%), acetamide (170 mg, 2.88 mmol), K_3PO_4 (450 mg, 2.12 mmol), evacuated and
 15 backfilled with argon. *trans*-*N,N'*-Dimethyl-1,2-cyclohexanediamine (17 μ L, 0.108 mmol, 10 mol%), iodobenzene (115 μ L, 1.03 mmol) and toluene (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 60 °C for 4 h. After the resulting suspension was allowed to reach room
 temperature, ethyl acetate (1 mL) and dodecane (235 μ L, internal GC standard) were added.
 20 GC analysis indicated 100% yield of the desired product.

Example 133

Preparation of *N,N*-diphenylformamide using ethylenediamine as the ligand at 80 °C for 4 h



A 15 mL resealable Schlenk tube was charged with CuI (9.8 mg, 0.0515 mmol, 5.0 mol%), *N*-phenylformamide (150 mg, 1.24 mmol), K_3PO_4 (450 mg, 2.12 mmol), evacuated and backfilled with argon. Ethylenediamine (7.0 μ L, 0.105 mmol, 10 mol%), iodobenzene (115 μ L, 1.03 mmol) and toluene (1.0 mL) were added under argon. The Schlenk tube was
 25

sealed with a Teflon valve and the reaction mixture was stirred at 80 °C for 4 h. The resulting suspension was allowed to reach room temperature and then filtered through a 0.5×1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2×15 cm, hexane-ethyl acetate 2:1, 15 mL fractions). Fractions 10-18 provided 188 mg (93% yield) of the desired product as a white solid.

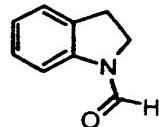
Example 134

Preparation of N,N-diphenylformamide using 1,2-diaminopropane as the ligand at 80 °C for 4 h

10 A 15 mL resealable Schlenk tube was charged with CuI (9.8 mg, 0.0515 mmol, 5.0 mol%), N-phenylformamide (150 mg, 1.24 mmol), K₃PO₄ (450 mg, 2.12 mmol), evacuated and backfilled with argon. 1,2-Diaminopropane (9.0 μL, 0.106 mmol, 10 mol%), iodobenzene (115 μL, 1.03 mmol) and toluene (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 80 °C for 4 h. After the resulting suspension was allowed to reach room temperature, ethyl acetate (1 mL) and dodecane (235 μL, internal GC standard) were added. GC analysis indicated 91% yield of the desired product.

Example 135

N-Formylindoline



20

A 15 mL resealable Schlenk tube was charged with CuI (9.6 mg, 0.0504 mmol, 5.0 mol%), N-formyl-2-(2-bromophenyl)ethylamine (229 mg, 1.00 mmol), K₂CO₃ (280 mg, 2.03 mmol), evacuated and backfilled with argon. *trans*-N,N'-Dimethyl-1,2-cyclohexanediamine (16 μL, 0.102 mmol, 10 mol%) and toluene (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 80 °C for 23 h. The resulting suspension was allowed to reach room temperature and then filtered through a 0.5×1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica

gel (2×10 cm, hexane-ethyl acetate 3:2, 15 mL fractions). Fractions 13-23 provided 145 mg (99% yield) of the desired product as a light yellow solid.

Example 136

Preparation of N-formylindoline from an aryl bromide at room temperature

5 The procedure above was followed exactly except that the reaction was performed at 25 °C for 24 h. The resulting suspension was filtered through a 0.5×1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2×15 cm, hexane-ethyl acetate 1:1, 15 mL fractions). Fractions 12-21 provided 107 mg (73% yield) of the desired product as a light
10 yellow solid.

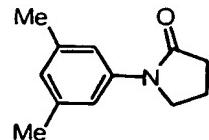
Example 137

Preparation of N-formylindoline from an aryl chloride at 80 °C

A 15 mL resealable Schlenk tube was charged with CuI (9.6 mg, 0.0504 mmol, 5.0 mol%), *N*-formyl-2-(2-chlorophenyl)ethylamine (184 mg, 1.00 mmol), K₂CO₃ (280 mg, 2.03 mmol), evacuated and backfilled with argon. *trans*-*N,N'*-Dimethyl-1,2-cyclohexanediamine (16 μL, 0.102 mmol, 10 mol%) and toluene (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 80 °C for 22 h. The resulting suspension was allowed to reach room temperature and then filtered through a 0.5×1 cm pad of silica gel eluting with 10 mL of ethyl acetate.
15
20 The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2×15 cm, hexane-ethyl acetate 1:1, 15 mL fractions). Fractions 13-20 provided 105 mg (71% yield) of the desired product as a white solid.

Example 138

Preparation of N-(3,5-dimethylphenyl)-2-pyrrolidinone using 2,6-dimethylphenol as the ligand



A 15 mL resealable Schlenk tube was charged with CuI (9.5 mg, 0.0499 mmol, 5.0 mol%), 2,6-dimethylphenol (25 mg, 0.205 mmol, 20 mol%), K₃PO₄ (440 mg, 2.07 mmol), evacuated and backfilled with argon. 5-Iodo-*m*-xylene (145 μL, 1.00 mmol), 2-

pyrrolidinone (95 μ L, 1.25 mmol) and toluene (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 110 °C for 21 h. The resulting suspension was allowed to reach room temperature and then filtered through a 0.5×1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was 5 concentrated and the residue was purified by flash chromatography on silica gel (2×20 cm, hexane-ethyl acetate 2:3, 15 mL fractions). Fractions 13-24 provided 180 mg (95% yield) of the desired product as a white solid.

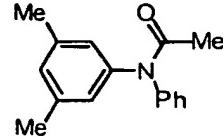
Example 139

10 **Preparation of N-(3,5-dimethylphenyl)-2-pyrrolidinone using n-hexylamine as the ligand/solvent at 80 °C**

A 15 mL resealable Schlenk tube was charged with CuI (9.5 mg, 0.0499 mmol, 5.0 mol%), K₃PO₄ (440 mg, 2.07 mmol), evacuated and backfilled with argon. 5-Iodo-*m*-xylene (145 μ L, 1.00 mmol), 2-pyrrolidinone (95 μ L, 1.25 mmol) and *n*-hexylamine (0.94 mL, 7.12 mmol) were added under argon. The Schlenk tube was sealed with a Teflon valve 15 and the reaction mixture was stirred at 80 °C for 23 h. The resulting brown suspension was allowed to reach room temperature and then filtered through a 0.5×1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2×10 cm, hexane-ethyl acetate 2:3, 10 mL fractions). Fractions 9-19 provided 185 mg (98% yield) of the desired product as a pale tan 20 solid.

Example 140

Preparation of N-(3,5-dimethylphenyl)-N-phenylacetamide using 2,6-dimethyl-phenol as the ligand



25 A 15 mL resealable Schlenk tube was charged with CuI (9.5 mg, 0.0499 mmol, 5.0 mol%), 2,6-dimethylphenol (25 mg, 0.205 mmol, 20 mol%), acetanilide (165 mg, 1.22 mmol), K₃PO₄ (440 mg, 2.07 mmol), evacuated and backfilled with argon. 5-Iodo-*m*-xylene (145 μ L, 1.00 mmol) and toluene (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 110 °C for 21 h.

The resulting suspension was allowed to reach room temperature and then filtered through a 0.5×1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2×15 cm, hexane-ethyl acetate 2:1, 15 mL fractions). Fractions 12-20 provided 133 mg (56% yield) of the desired product as a yellow solid.

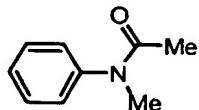
5 **Example 141**

Preparation of N-(3,5-dimethylphenyl)-N-phenylacetamide using n-hexylamine as the ligand and solvent

A 15 mL resealable Schlenk tube was charged with CuI (9.5 mg, 0.0499 mmol, 5.0 mol%), acetanilide (165 mg, 1.22 mmol), K₃PO₄ (440 mg, 2.07 mmol), evacuated and backfilled with argon. 5-Iodo-*m*-xylene (145 μL, 1.00 mmol) and *n*-hexylamine (0.94 mL, 7.12 mmol) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 100 °C for 21 h. The resulting pale yellow suspension was allowed to reach room temperature and then filtered through a 0.5×1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2×15 cm, hexane-ethyl acetate 2:1, 15 mL fractions). Fractions 12-20 provided 205 mg (86% yield) of the desired product as a pale yellow solid.

10 **Example 142**

15 **Preparation of N-methyl-N-phenylacetamide using n-hexylamine as the ligand**

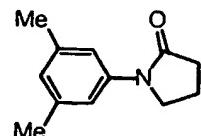


A 15 mL resealable Schlenk tube was charged with CuI (9.5 mg, 0.0499 mmol, 5.0 mol%) and K₃PO₄ (430 mg, 2.03 mmol), evacuated and backfilled with argon. Iodobenzene (112 μL, 1.00 mmol), *N*-methylacetamide (0.46 mL, 6.00 mmol) and *n*-hexylamine (0.53 mL, 4.01 mmol) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 110 °C for 21 h. The resulting white suspension was allowed to reach room temperature and then filtered through a 0.5×1 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2×15 cm, hexane-ethyl acetate 2:3, 15 mL fractions).

fractions). Fractions 12-20 provided 136 mg (91% yield) of the desired product as a pale tan solid.

Example 143

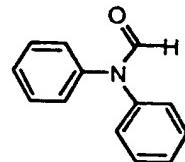
- 5 Preparation of *N*-(3,5-dimethylphenyl)-2-pyrrolidinone using *tert*-butylimino-tris(pyrrolidino)-phosphorane as the base



A 15 mL resealable Schlenk tube was charged with CuI (9.5 mg, 0.0499 mmol, 5.0 mol%), evacuated and backfilled with argon. *trans*-*N,N'*-Dimethyl-1,2-cyclohexanediamine (16 μ L, 0.102 mmol, 10 mol%), 5-iodo-*m*-xylene (145 μ L, 1.00 mmol), 2-pyrrolidinone (95 μ L, 1.25 mmol), *tert*-butylimino-tris(pyrrolidino)phosphorane (0.62 mL, 2.03 mmol), and toluene (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 90 °C for 21 h. The resulting clear, dark brown solution was allowed to reach room temperature and then filtered through a 0.5×2 cm pad of silica gel eluting with 10 mL of ethyl acetate. The filtrate was concentrated and the residue 10 was purified by flash chromatography on silica gel (2×15 cm, hexane-ethyl acetate 2:3, 15 mL fractions). Fractions 10-19 provided 180 mg (95% yield) of the desired product as a white solid.

Example 144

- 20 Preparation of *N,N*-diphenylformamide using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as the base

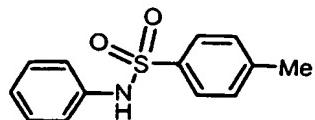


A 15 mL resealable Schlenk tube was charged with CuI (9.6 mg, 0.0504 mmol, 5.0 mol%), *N*-phenylformamide (146 mg, 1.21 mmol), evacuated and backfilled with argon. *trans*-*N,N'*-Dimethyl-1,2-cyclohexanediamine (16 μ L, 0.102 mmol, 10 mol%), iodobenzene (112 μ L, 1.00 mmol), toluene (1.0 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 0.45 mL, 3.01 mmol) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 100 °C for 22 h. After the resulting clear solution 25

ethyl acetate. The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2×15 cm, hexane-ethyl acetate 4:1, 15 mL fractions). Fractions 10-17 provided 244 mg (89% yield) of the desired product.

Example 149

- 5 Preparation of N-phenyl-p-toluenesulfonamide using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as the base



A 15 mL resealable Schlenk tube was charged with CuI (9.6 mg, 0.0504 mmol, 5.0 mol%), *p*-toluenesulfonamide (205 mg, 1.20 mmol), evacuated and backfilled with argon. 10 *trans*-*N,N'*-Dimethyl-1,2-cyclohexanediamine (16 μL, 0.102 mmol, 10 mol%), iodobenzene (112 μL, 1.00 mmol), toluene (1.0 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 0.45 mL, 3.01 mmol) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 100 °C for 22 h. The resulting clear solution was allowed to cool to room temperature, poured into aq NH₄Cl solution and extracted with 15 3×15 mL of CH₂Cl₂. The combined organic phases were dried (Na₂SO₄), concentrated, and the residue was purified by flash chromatography on silica gel (2×15 cm, hexane-ethyl acetate 3:1, 15 mL fractions). Fractions 9-15 provided 60 mg (24% yield) of the desired product as a white solid.

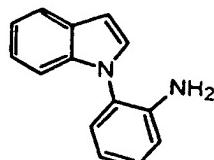
Example 150

- 20 General procedure for the arylation of N-H heterocycles using *trans*-*N,N'*-dimethyl-1,2-cyclohexanediamine as ligand

To a flame-dried resealable Schlenk tube, or alternatively a resealable test tube, was added CuI (5 mol%), the heterocycle (1.0 mmol) and base (2.1 mmol). The Schlenk tube was fixed with a rubber septum, evacuated twice and back-filled with argon. Dodecane (45 25 μL, 0.20 mmol), the aryl halide (1.2 mmol), *trans*-*N,N'*-dimethyl-1,2-cyclohexanediamine (10-20 mol%) and the respective solvent (1 mL) were then added successively under argon. The reaction tube was sealed and the contents were stirred with heating via an oil bath at 110 °C for 24 hours. The reaction mixture was cooled to ambient temperature, diluted with 2-3 mL ethyl acetate, and filtered through a plug of silica gel eluting with 10-20 mL of ethyl

acetate. The filtrate was concentrated and the resulting residue was purified by column chromatography to provide the desired product.

1-(2-Aminophenyl)indole

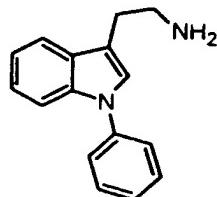


- 5 Using the general procedure, indole (0.117 g, 1.00 mmol) was coupled with 2-bromoaniline (0.206 g, 1.20 mmol) using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), K₃PO₄ (2.1 mmol), *trans*-N,N'-dimethyl-1,2-cyclohexanediamine (16 μL, 0.10 mmol, 10 mol%) and toluene (1.0 mL) to give the crude product. Column chromatography (2×15 cm, hexane:ethyl acetate 5:1) provided 0.148 g (71% yield) of the product as a colorless oil.
- 10 ¹H NMR (400 MHz, CDCl₃): δ 7.64 (m, 1H), 7.18 (m, 6H), 6.82 (m, 2H), 6.64 (m, 1H), 3.52 (bs, 2H).

Preparation of 1-(2-aminophenyl)indole at 80 °C

- Using the general procedure, indole (0.117 g, 1.00 mmol) was coupled at 80 °C with 2-iodoaniline (0.263 g, 1.20 mmol) using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), K₃PO₄ (2.1 mmol), *trans*-N,N'-dimethyl-1,2-cyclohexanediamine (32 μL, 0.20 mmol, 20 mol%) and toluene (1.0 mL) to give the crude product. The above product was identified by comparison (GC) to a previously prepared sample and the GC yield was determined to be 92%.

1-Phenyltryptamine

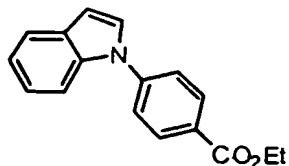


- 20 Using the general procedure, tryptamine (0.160 g, 1.00 mmol) was coupled with iodobenzene (134 μL, 1.20 mmol) using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), K₃PO₄ (2.1 mmol), *trans*-N,N'-dimethyl-1,2-cyclohexanediamine (32 μL, 0.20 mmol, 20 mol%) and toluene (1.0 mL) to give the crude product. Column chromatography (2×15 cm, methylene chloride (saturated with ammonia):methanol 50:1) provided 0.206 g (87% yield) of the

product as a yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 7.65 (m, 1H), 7.55 (m, 1H), 7.47 (m, 4H), 7.31 (m, 1H), 7.18 (m, 3H), 3.06 (t, $J = 7$ Hz, 2H), 2.94 (t, $J = 7$ Hz, 2H), 1.40 (bs, 2H).

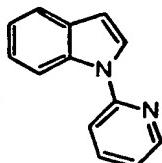
Preparation of 1-(4-ethoxycarbonylphenyl)indole at 80 °C

5



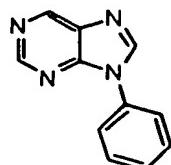
Using the general procedure, indole (0.117 g, 1.00 mmol) was coupled at 80 °C with ethyl-4-iodobenzoate (0.331 g, 1.20 mmol) using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), K_3PO_4 (2.1 mmol), *trans*-*N,N'*-dimethyl-1,2-cyclohexanediamine (32 μL , 0.20 mmol, 20 mol%) and toluene (1.0 mL) to give the crude product. The above product was identified by comparison (GC) to a previously prepared sample and the GC yield was determined to be 96%.

Preparation of 1-(2-pyridyl)indole from 2-chloropyridine



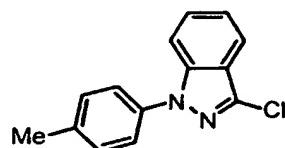
Using the general procedure, indole (0.117 g, 1.00 mmol) was coupled with 2-chloropyridine (113 μL , 1.20 mmol) using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), K_3PO_4 (2.1 mmol), *trans*-*N,N'*-dimethyl-1,2-cyclohexanediamine (32 μL , 0.20 mmol, 20 mol%) and toluene (1.0 mL) to give the crude product. Column chromatography (2×15 cm, hexane:ethyl acetate 9:1) provided 0.194 g (100% yield) of the product as a yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 9.24 (s, 1H), 9.05 (s, 1H), 8.41 (s, 1H), 7.75 (m, 2H), 7.60 (m, 2H), 7.48 (m, 1H).

J-Phenylpurine



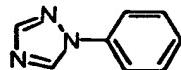
Using the general procedure, purine (0.120 g, 1.00 mmol) was coupled with iodobenzene (225 μ L, 2.00 mmol) using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), Cs₂CO₃ (2.1 mmol), *trans*-*N,N'*-dimethyl-1,2-cyclohexanediamine (32 μ L, 0.20 mmol, 20 mol%) and dimethylformamide (1.0 mL) to give the crude product. Column chromatography (2 \times 15 cm, 5 hexane:ethyl acetate 1:2) provided 0.136 g (69% yield) of the product as a white solid. ¹H NMR (400 MHz, CDCl₃): δ 8.00 (d, *J* = 0.9 Hz, 1H), 7.52 (m, 3H), 7.42 (m, 5H), 6.73 (dd, *J* = 0.6 Hz and *J* = 3.3 Hz, 1H), 7.60 (m, 2H), 7.48 (m, 1H).

I-(4-Methylphenyl)-3-chloroindazole

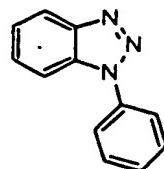


10 Using the general procedure, 3-chloroindazole (0.153 g, 1.00 mmol) was coupled with 4-bromotoluene, (148 μ L, 1.20 mmol) using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), K₃PO₄ (2.1 mmol), *trans*-*N,N'*-dimethyl-1,2-cyclohexanediamine (32 μ L, 0.20 mmol, 20 mol%) and toluene (1.0 mL) to give the crude product. Column chromatography (2 \times 15 cm, hexane:ethyl acetate 50:1) provided 0.211 g (87% yield) of the product as a colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 7.70 (d, *J* = 8.2 Hz, 1H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.52 (m, 2H), 7.43 (m, 1H), 7.24 (d, *J* = 8.2 Hz, 2H), 7.22 (m, 1H), 2.38 (s, 3H).

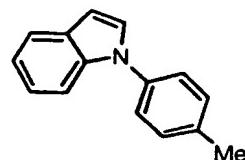
I-Phenyl-1,2,4-triazole



20 Using the general procedure, 1,2,4-triazole (0.069 g, 1.00 mmol) was coupled with iodobenzene (134 μ L, 1.20 mmol) using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), K₃PO₄ (2.1 mmol), *trans*-*N,N'*-dimethyl-1,2-cyclohexanediamine (16 μ L, 0.10 mmol, 10 mol%) and dimethylformamide (1.0 mL) to give the crude product. Column chromatography (2 \times 15 cm, hexane:ethyl acetate 3:1) provided 0.135 g (93% yield) of the product as a white solid. ¹H NMR (400 MHz, CDCl₃): δ 8.58 (s, 1H), 8.10 (s, 1H), 7.66 (m, 2H), 7.47 (m, 2H), 7.37 (m, 1H).

I-Phenylbenzotriazole

Using the general procedure, benzotriazole (0.119 g, 1.00 mmol) was coupled with iodobenzene (134 μ L, 1.20 mmol) using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), K_3PO_4 (2.1 mmol), *trans*-*N,N'*-dimethyl-1,2-cyclohexanediamine (16 μ L, 0.10 mmol, 10 mol%) and dimethylformamide (1.0 mL) to give the crude product. Column chromatography (2x15 cm, hexane:ethyl acetate 9:1) provided 0.186 g (95% yield) of the product as a white solid. 1H NMR (400 MHz, $CDCl_3$): δ 8.17 (m, 1H), 7.78 (m, 3H), 7.62 (m, 2H), 7.55 (m, 2H), 7.42 (m, 1H).

10 *Example 151*Preparation of 1-(4-methylphenyl)indole using *N,N'*-dimethylethylenediamine as ligand

To a flame-dried resealable Schlenk tube was added CuI (0.002 g, 0.01 mmol), indole (0.141 g, 1.20 mmol) and K_3PO_4 (0.446 g, 2.1 mmol), the Schlenk tube was 15 evacuated twice and back-filled with argon. Dodecane (45 μ L, 0.20 mmol), 4-bromotoluene (123 μ L, 1.00 mmol), *N,N'*-dimethylethylenediamine (11 μ L, 0.10 mmol) and toluene (1 mL) were then added successively under argon. The reaction tube was sealed and the contents were stirred with heating via an oil bath at 110 °C for 24 hours. The reaction mixture was cooled to ambient temperature, diluted with 2-3 mL ethyl acetate, and 20 filtered through a plug of silica gel eluting with 10-20 mL of ethyl acetate. Comparison to authentic material showed that the product was formed in a 92% GC yield.

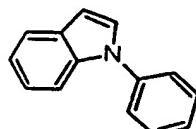
*Example 152*Preparation of 1-(4-methylphenyl)indole using *N*-methylethylenediamine as ligand

To a flame-dried resealable Schlenk tube was added CuI (0.002 g, 0.01 mmol), 25 indole (0.141 g, 1.20 mmol) and K_3PO_4 (0.446 g, 2.1 mmol), the Schlenk tube was evacuated twice and back-filled with argon. Dodecane (45 μ L, 0.20 mmol), 4-

bromotoluene (123 μ L, 1.00 mmol), *N*-methylethylenediamine (9 μ L, 0.10 mmol) and toluene (1 mL) were then added successively under argon. The reaction tube was sealed and the contents were stirred with heating via an oil bath at 110 °C for 24 hours. The reaction mixture was cooled to ambient temperature, diluted with 2-3 mL ethyl acetate, and 5 filtered through a plug of silica gel eluting with 10-20 mL of ethyl acetate. Comparison to authentic material showed that the product was formed in a 99% GC yield.

Example 153

Preparation of 1-phenylindole in air



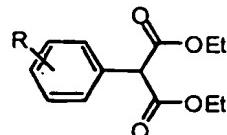
10 To a flame-dried resealable test tube was added CuI (0.002 g, 0.01 mmol), indole (0.117 g, 1.00 mmol) and K₃PO₄ (0.446 g, 2.1 mmol). A rubber septum was fitted and dodecane (45 μ L, 0.20 mmol), iodobenzene (134 μ L, 1.20 mmol), *trans*-*N,N*'-dimethyl-1,2-cyclohexanediamine (16 μ L, 0.10 mmol) and toluene (1 mL) were added successively in air. The reaction tube was sealed and the contents were stirred with heating via an oil bath at 110 °C for 24 hours. The reaction mixture was cooled to ambient temperature, diluted with 2-3 mL ethyl acetate, and filtered through a plug of silica gel eluting with 10-20 mL of ethyl acetate. Comparison to authentic material showed that the product was formed in an 82% 15 GC yield.

Example 154

20 Preparation of 1-phenylindole using various copper sources

To a flame-dried resealable test tube was added the copper source (0.050 mmol), indole (0.117 g, 1.00 mmol) and K₃PO₄ (0.446 g, 2.1 mmol) under an atmosphere of argon. A rubber septum was fitted and dodecane (45 μ L, 0.20 mmol), iodobenzene (134 μ L, 1.20 mmol), *trans*-*N,N*'-dimethyl-1,2-cyclohexanediamine (16 μ L, 0.10 mmol) and toluene (1 mL) were added successively under a stream of argon. The reaction tube was sealed and the 25 contents were stirred with heating via an oil bath at 110 °C for 24 hours. The reaction mixture was cooled to ambient temperature, diluted with 2-3 mL ethyl acetate, and filtered through a plug of silica gel eluting with 10-20 mL of ethyl acetate. The GC yields of the desired product are tabulated below.

Copper source	GC yield 1-phenylindole
Cu (copper bronze)	99%
CuI	100%
CuCl ₂	100%
Cu(OAc) ₂	100%
Cu(OMe) ₂	98%

Example 155General Procedure for Malonate Arylation Using Aryl Iodides

An oven-dried Schlenk tube equipped with a magnetic stirbar and a Teflon stopcock was evacuated while hot and allowed to cool under argon. The tube was charged with CuI (9.6 mg, 5.0 mol %), 2-hydroxybiphenyl (17.1 mg, 10.0 mol %), Cs₂CO₃ (0.490 mg, 1.50 mmol), and the aryl iodide (if a solid, 1.0 mmol). The tube was evacuated and backfilled 10 with argon (3 times), and the Teflon stopcock was replaced with a rubber septum. The aryl iodide (if liquid) was added volumetrically (1.0 mmol), followed by diethyl malonate (304 µL, 2.00 mmol) and anhydrous THF (1.0 mL). The septum was replaced by the Teflon stopcock under a positive pressure of argon, and the sealed tube was placed in an oil bath preheated to 70 °C. After the designated time period, the reaction was allowed to cool to 15 room temperature and was then partitioned between 20 mL ethyl acetate and 10 mL saturated NH₄Cl (*aq*). The organic portion was dried (Na₂SO₄), filtered through Celite, and concentrated on a rotary evaporator. The oil thus obtained was purified by silica gel chromatography to give the product α-aryl malonate.

20 *Phenyl diethyl malonate* Obtained as a colorless oil (217 mg, 92%); reaction time 24 h.

4-Methoxyphenyl diethyl malonate

Obtained as a colorless oil (227 mg, 87%); reaction time 30 h.

4-Chlorophenyl diethyl malonate

Obtained as a colorless oil (265 mg, 97%); reaction time 24 h.

1-Naphthyl diethyl malonate

Obtained as a pale yellow solid (280 mg, 98%); reaction time 30 h.

3-Trifluoromethylphenyl diethyl malonate

5 Obtained as a colorless oil (267 mg, 88%); reaction time 24 h.

2-Isopropylphenyl diethyl malonate

Obtained as a pale yellow oil (238 mg, 86%); reaction time 31 h (10 mol % CuI used in reaction).

2,4-Dimethoxyphenyl diethyl malonate

10 Obtained as a tan solid (269 mg, 91%); reaction time 30 h.

3-Ethoxycarbonylphenyl diethyl malonate

Obtained as a colorless oil (265 mg, 86%) reaction time 24 h.

4-Aminophenyl diethyl malonate

Obtained as a yellow oil (200 mg, 79%); reaction time 30 h.

15 *4-Hydroxyphenyl diethyl malonate*

Obtained as a colorless solid (191 mg, 73%); reaction time 30 h (2.5 equiv Cs₂CO₃ used in reaction).

4-N-Acetyl aminophenyl diethyl malonate

Obtained as a colorless solid (214 mg, 72%); reaction time 30 h (10 mol % CuI used in reaction).

3-Nitrophenyl diethyl malonate

Obtained as a yellow oil (240 mg, 85%); reaction time 24 h.

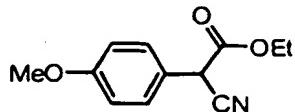
3-Cyanophenyl diethyl malonate

Obtained as a colorless oil (194 mg, 73%); reaction time 24 h.

25 **Example 156**

General Procedure for Malonate Arylation using Aryl Bromides

- ~ An oven-dried Schlenk tube equipped with a magnetic stirbar and a Teflon stopcock was evacuated while hot and allowed to cool under argon. The tube was charged with CuI (9.6 mg, 5.0 mol %), 8-hydroxyquinoline (14.5 mg, 10.0 mol %), and Cs₂CO₃ (0.490 mg, 1.50 mmol). The tube was evacuated and backfilled with argon (3 times), and the Teflon stopcock was replaced with a rubber septum. The aryl bromide was added volumetrically (1.0 mmol), followed by the malonate (2.00 mmol) and anhydrous dioxane (1.0 mL). The

Example 158**Arylation of Ethyl Cyanoacetate**

- An oven-dried Schlenk tube equipped with a magnetic stirbar and a Teflon stopcock
 5 was evacuated while hot and allowed to cool under argon. The tube was charged with CuI
 (9.6 mg, 5.0 mol %), 1,10-phenanthroline (10.9 mg, 5.5 mol %), Cs₂CO₃ (0.490 mg, 1.50
 mmol), and 4-iodoanisole (0.230 g, 0.98 mmol). The tube was evacuated and backfilled
 with argon (3 times), and the Teflon stopcock was replaced with a rubber septum. Ethyl
 cyanoacetate (0.13 mL, 1.22 mmol) was added, followed by anhydrous dioxane (1.0 mL).
 10 The septum was replaced by the Teflon stopcock under a positive pressure of argon, and the
 sealed tube was placed in an oil bath preheated to 110 °C. After the designated time, the
 reaction was allowed to cool to room temperature, and was then partitioned between 20 mL
 ethyl acetate and 10 mL saturated NH₄Cl (*aq*). The organic portion was dried (Na₂SO₄),
 filtered through Celite, and concentrated on a rotary evaporator. The oil thus obtained was
 15 purified by silica gel chromatography to give the product 4-methoxyphenyl ethyl
 cyanoacetate as a yellow oil (132 mg, 61%).

Example 159**Vinylation of indole using *trans*-N,N'-dimethyl-1,2-cyclohexanediamine as the ligand****General Procedure**

- 20 To a resealable test tube was added a stir bar, CuI (5 mol%), indole (1.00 mmol) and
 base (2.1 mmol). The tube was then fixed with a rubber septum, and evacuated and back-
 filled with argon twice. Dodecane (45 µL, 0.20 mmol), the vinyl halide (1.2 mmol), *trans*-
N,N'-dimethyl-1,2-cyclohexanediamine (10 mol%) and toluene (1 mL) were then added
 successively under argon. The septum was replaced with a screw cap and the contents were
 25 stirred at the desired temperature (oil bath, if needed) for 24 hours. The reaction mixture
 was allowed to reach ambient temperature, diluted with 2-3 mL ethyl acetate, shaken, and
 allowed to settle for a few min before the top layer was sampled for GC and GC/MS
 analysis.

septum was replaced by the Teflon stopcock under a positive pressure of argon, and the sealed tube was placed in an oil bath preheated to 110 °C. After the designated time period, the reaction was allowed to cool to room temperature and was treated with *n*-undecane (105.6 µL, 0.50 mmol) prior to partitioning between 20 mL ethyl acetate and 10 mL saturated NH₄Cl (*aq*). The organic portion was analyzed by GC and/or GC-MS. GC yield of product was determined using response factors obtained from previously isolated product.

4-Methoxyphenyl dimethyl malonate

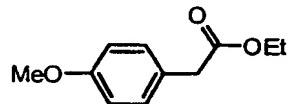
After 19.5 hours, a GC yield of 43% was obtained.

10 **4-Trifluoromethylphenyl diethyl malonate**

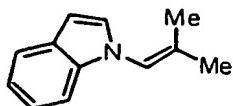
After 20.5 hours, GC-MS indicated complete conversion of the aryl bromide to the title compound in addition to the decarboxylated malonate product, 4-trifluoromethylphenyl ethyl acetate.

Example 157

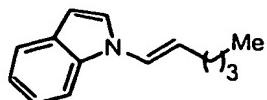
15 **Synthesis of α-Aryl Acetates**



An oven-dried Schlenk tube equipped with a magnetic stirbar and a Teflon stopcock was evacuated while hot and allowed to cool under argon. The tube was charged with CuI (9.6 mg, 5.0 mol %), 1,10-phenanthroline (10.9 mg, 5.5 mol %), Cs₂CO₃ (0.490 mg, 1.50 mmol), and 4-iodoanisole (0.226 g, 0.97 mmol). The tube was evacuated and backfilled with argon (3 times), and the Teflon stopcock was replaced with a rubber septum. Ethyl acetoacetate was added (0.15 mL, 1.18 mmol), followed by anhydrous dioxane (1.0 mL). The septum was replaced by the Teflon stopcock under a positive pressure of argon, and the sealed tube was placed in an oil bath preheated to 110 °C. After 24 h, the reaction was allowed to cool to room temperature, and was then partitioned between 20 mL ethyl acetate and 10 mL saturated NH₄Cl (*aq*). The organic portion was dried (Na₂SO₄), filtered through Celite, and concentrated on a rotary evaporator. The oil thus obtained was purified by silica gel chromatography to give the product 4-methoxyphenyl ethyl acetate as a colorless oil (106 mg, 56%).

1-(2-Methylpropenyl)indole

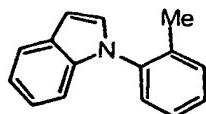
Using the general procedure described above, indole (0.117 g, 1.00 mmol) was coupled with 1-bromo-2-methylpropene (123 μ L, 1.20 mmol) using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), K_3PO_4 (2.1 mmol), *trans*-*N,N*-dimethyl-1,2-cyclohexanediamine (16 μ L, 0.10 mmol, 10 mol%) and toluene (1.0 mL) at 80 °C to give 45-50% conversion of indole (GC); the structure of the product was assigned using GC/MS analysis.

1-(1-Hexenyl)indole

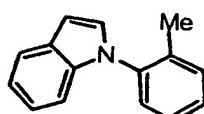
Using the general procedure described above, indole (0.117 g, 1.00 mmol) was coupled with 1-iodo-1-hexene (171 μ L, 1.20 mmol) using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), K_3PO_4 (2.1 mmol), *trans*-*N,N*-dimethyl-1,2-cyclohexanediamine (16 μ L, 0.10 mmol, 10 mol%) and toluene (1.0 mL) at ambient temperature to give 42% conversion of indole (GC); the structure of the product was assigned by GC/MS analysis.

Example 160**Arylation of indole using 2-(aminomethyl)pyridine or *N,N*-diethylsalicylamide as the ligand**

To a resealable test tube was added a stir bar, CuI (5 mol%), indole (1.00 mmol) and K_3PO_4 (2.1 mmol). The tube was then fixed with a rubber septum, and evacuated and back-filled with argon twice. Dodecane (45 μ L, 0.20 mmol), the vinyl halide (1.2 mmol), ligand (20 mol%) and toluene (1 mL) were then added successively under argon. The septum was replaced with a screw cap and the contents were stirred at 110 °C (oil bath) for 24 hours. The reaction mixture was allowed to reach ambient temperature, diluted with 2-3 mL ethyl acetate, shaken, and allowed to settle for a few minutes. The top layer was then analyzed by GC and GC/MS.

1-(2-Methylphenyl)indole

Using the general procedure described above, indole (0.117 g, 1.00 mmol) was coupled with 2-bromotoluene (144 μ L, 1.20 mmol) using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), K₃PO₄ (2.1 mmol), 2-(aminomethyl)pyridine (21 μ L, 0.20 mmol, 20 mol%) and toluene (1.0 mL) to give 38% conversion of indole (GC). The structure of the product (35% GC yield) was assigned by comparison of the GC to authentic material.

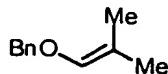
1-(2-Methylphenyl)indole

Using the general procedure described above, indole (0.117 g, 1.00 mmol) was coupled with 2-bromotoluene (144 μ L, 1.20 mmol) using CuI (9.5 mg, 0.050 mmol, 5.0 mol%), K₃PO₄ (2.1 mmol), *N,N*-diethylsalicylamide (0.039 g, 0.20 mmol, 20 mol%) and toluene (1.0 mL) to give 42% conversion of indole (GC). The structure of the product (40% GC yield) was assigned by comparison of the GC to authentic material.

Example 161E-1-Benzylxyhex-1-ene from benzyl alcohol and E-1-iodohexene

A screw cap test tube was charged with benzyl alcohol (207 μ L, 2.00 mmol), *E*-1-iodohexene (210 mg, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), 1,10-phenanthroline (36.0 mg, 0.200 mmol), Cs₂CO₃ (489 mg, 1.50 mmol) and toluene (500 μ L). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 80 °C for 14 hours. The resulting suspension was allowed to reach room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with dichloromethane. The filtrate was concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane/CH₂Cl₂ 10:1) provided 136 mg (72% yield) of the title compound as a colorless liquid.

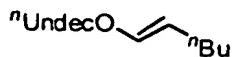
Example 1621-Benzylxy-2-methylpropene from benzyl alcohol and 1-bromo-2-methylpropene



- A screw cap test tube was charged with benzyl alcohol (207 µL, 2.00 mmol), 1-bromo-2-methylpropene (103 µL, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), 1,10-phenanthroline (36.0 mg, 0.200 mmol), Cs₂CO₃ (489 mg, 1.50 mmol) and toluene (500 µL).
- 5 The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 80 °C for 48 hours. The resulting suspension was allowed to reach room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with dichloromethane. The filtrate was concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane/CH₂Cl₂ 10:1) provided 81 mg (50% yield) of the title compound as a colorless oil.
- 10

Example 163

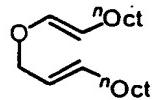
E-1-Undecyloxy-hex-1-ene from n-undecanol and E-1-iodohexene



- A screw cap test tube was charged with *n*-undecanol (415 µL, 2.00 mmol), *E*-1-iodohexene (210 mg, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), 1,10-phenanthroline (36.0 mg, 0.200 mmol), Cs₂CO₃ (489 mg, 1.50 mmol) and toluene (500 µL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 100°C for 36 hours. The resulting suspension was allowed to reach room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with dichloromethane. The filtrate was concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane/CH₂Cl₂ 20:1) provided 141 mg (55% yield) of the title compound as a colorless liquid.
- 15
- 20

Example 164

1*E*,2*E*-1-Dec-1-enyloxyundec-2-ene from E-2-undecene-1-ol and E-1-iododecene



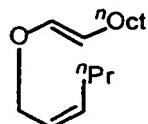
- 25 A screw cap test tube was charged with *E*-2-undecene-1-ol (401 µL, 2.00 mmol), *E*-1-iododecene (266 mg, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), 3,4,7,8-tetramethyl-1,10-phenanthroline (47.3 mg, 0.200 mmol), Cs₂CO₃ (489 mg, 1.50 mmol) and toluene (500 µL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically

and heated at 80°C for 24 hours. The resulting suspension was allowed to reach room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with dichloromethane. The filtrate was concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane/CH₂Cl₂ 100:1) provided 141 mg (199 mg, 68% yield) of the title compound as a colorless oil.

5

Example 165

1*E*,2*Z*-1-Hex-2-enyloxydec-1-ene from Z-2-hexen-1-ol and *E*-1-iododecene



A screw cap test tube was charged with Z-2-hexene-1-ol (237 µL, 2.00 mmol), *E*-1-iododecene (266 mg, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), 3,4,7,8-tetramethyl-1,10-phenanthroline (47.3 mg, 0.200 mmol), Cs₂CO₃ (489 mg, 1.50 mmol) and toluene (500 µL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 90°C for 22 hours. The resulting suspension was allowed to reach room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with dichloromethane.

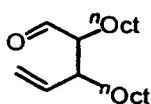
10

The filtrate was concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane/CH₂Cl₂ 100:1) provided 135 mg (57% yield) of the title compound as a colorless oil.

15

Example 166

2,3-Dioctyl-pent-4-enal from *E*-2-undecene-1-ol and *E*-1-iododecene



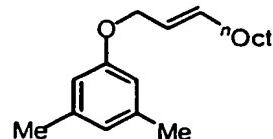
20

An oven dried screw cap test tube was charged with *E*-2-undecene-1-ol (401 µL, 2.00 mmol), *E*-1-iododecene (266 mg, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), 1,10-phenanthroline (36.0 mg, 0.200 mmol), Cs₂CO₃ (489 mg, 1.50 mmol) and *o*-xylene (500 µL). The test tube was evacuated and backfilled with argon (flushed for 10 min). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 140°C for 19 hours. The resulting suspension was allowed to reach room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with dichloromethane. The filtrate was

concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane/CH₂Cl₂ 3:1) provided 188 mg (64% yield) of the title compound as a yellow oil.

Example 167

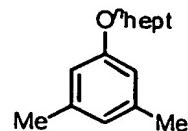
E-1,3-Dimethyl-5-undec-2-enyloxy-benzene from E-2-undecene-1-ol and 3,5-dimethylbromobenzene



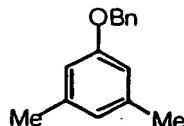
A screw cap test tube was charged with *E*-2-undecene-1-ol (401 µL, 2.00 mmol), 3,5-dimethylbromobenzene (136 µL, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), 3,4,7,8-tetramethyl-1,10-phenanthroline (47.3 mg, 0.200 mmol), Cs₂CO₃ (489 mg, 1.50 mmol) and *o*-xylene (500 µL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 120°C for 48 hours. The resulting suspension was allowed to reach room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with dichloromethane. The filtrate was concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane/CH₂Cl₂ 10:1) provided 128 mg (47% yield) of the title compound as a colorless oil.

Example 168

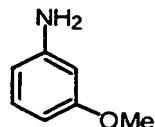
1-Heptoxy-3,5-methylbenzene from the corresponding arylbromide



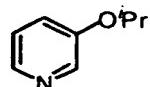
A screw cap test tube was charged with *n*-heptanol (1.0 mL), 3,5-dimethylbromobenzene (136 µL, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), 3,4,7,8-tetramethyl-1,10-phenanthroline (47.3 mg, 0.200 mmol) and Cs₂CO₃ (977 mg, 3.00 mmol). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 110 °C for 28 hours. The reaction mixture was allowed to reach room temperature. Dodecane (227 µL, 1.00 mmol; internal standard) was added and a GC sample was filtered through Celite and eluted with CH₂Cl₂. GC analysis revealed 51 % yield of the desired product.

Example 169**1-Benzyl-3,5-dimethylbenzene from benzyl alcohol and 3,5-dimethylbromobenzene**

A screw cap test tube was charged with benzyl alcohol (207 µL, 2.00 mmol), 3,5-dimethylbromobenzene (136 µL, 1.00 mmol), CuI (19.0 mg, 0.100 mmol), 3,4,7,8-tetramethyl-1,10-phenanthroline (47.3 mg, 0.200 mmol), Cs₂CO₃ (489 mg, 1.50 mmol) and *o*-xylene (500 µL). The test tube was sealed with a screw cap. The reaction mixture was stirred magnetically and heated at 120°C for 48 hours. The resulting suspension was allowed to reach room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with dichloromethane. The filtrate was concentrated. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane/CH₂Cl₂ 10:1) provided 135 mg (64% yield) of the title compound as a colorless oil.

Example 170**3-Methoxyaniline**

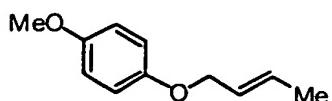
A test tube was charged with CuI (20 mg, 0.10 mmol, 0.10 equiv), 1,10-phenanthroline (36 mg, 0.20 mmol, 0.20 equiv), Cs₂CO₃ (456 mg, 1.4 mmol, 1.4 equiv), 3-iodoaniline (120 µL, 1.0 mmol, 1.0 equiv) and methanol (1.0 mL, 25 mmol, 25 equiv). The test tube was sealed and the reaction mixture was stirred at 110 °C for 21 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel, eluting with diethyl ether. The filtrate was concentrated in vacuo. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane:diethyl ether 2:1) provided 96 mg (78% yield) of the known title compound as a yellow oil.

Example 171**3-Isopropoxypyridine**

A test tube was charged with CuI (20 mg, 0.10 mmol, 0.10 equiv), 1,10-phenanthroline (36 mg, 0.20 mmol, 0.20 equiv), Cs₂CO₃ (652 mg, 2.0 mmol, 2.0 equiv), 3-iodopyridine (205 mg, 1.0 mmol, 1.0 equiv) and *iso*-propanol (1.0 mL, 13 mmol, 13 equiv). The test tube was sealed and the reaction mixture was stirred at 110 °C for 21 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel, eluting with diethyl ether. The filtrate was concentrated in vacuo. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane:diethyl ether 4:1) provided 126 mg (92% yield) of the title compound as a colorless oil.

Example 172

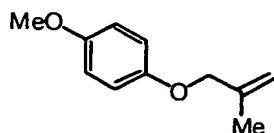
10 4-(*trans*-But-2-enyloxy)anisole



A test tube was charged with CuI (20 mg, 0.10 mmol, 0.10 equiv), 1,10-phenanthroline (36 mg, 0.20 mmol, 0.20 equiv), Cs₂CO₃ (652 mg, 2.0 mmol, 2.0 equiv), 4-iodoanisole (234 mg, 1.0 mmol, 1.0 equiv), *trans*-2-buten-1-ol (171 μL, 2.0 mmol, 2.0 equiv) and toluene (0.5 mL). The test tube was sealed and the reaction mixture was stirred at 110 °C for 22 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel, eluting with diethyl ether. The filtrate was concentrated in vacuo. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane:diethyl ether 30:1) provided 153 mg (86% yield) of the title compound as a light yellow oil.

Example 173

4-(2-Methylallyloxy)anisole

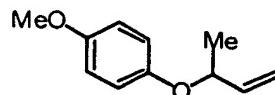


A test tube was charged with CuI (20 mg, 0.10 mmol, 0.10 equiv), 1,10-phenanthroline (36 mg, 0.20 mmol, 0.20 equiv), Cs₂CO₃ (652 mg, 2.0 mmol, 2.0 equiv), 4-iodoanisole (234 mg, 1.0 mmol, 1.0 equiv), 2-methyl-2-propen-1-ol (168 μL, 2.0 mmol, 2.0 equiv) and toluene (0.5 mL). The test tube was sealed and the reaction mixture was stirred at 110 °C for 28 h. The resulting suspension was cooled to room temperature and filtered

through a 0.5×1 cm pad of silica gel, eluting with diethyl ether. The filtrate was concentrated in vacuo. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane:diethyl ether 30:1) provided 139 mg (78% yield) of the title compound as a colorless solid.

5 **Example 174**

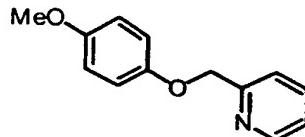
4-(1-Methylallyloxy)anisole



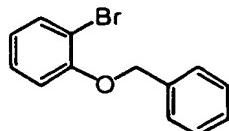
A test tube was charged with CuI (20 mg, 0.10 mmol, 0.10 equiv), 1,10-phenanthroline (36 mg, 0.20 mmol, 0.20 equiv), Cs₂CO₃ (652 mg, 2.0 mmol, 2.0 equiv), 4-iodoanisole (234 mg, 1.0 mmol, 1.0 equiv), 3-buten-2-ol (180 μ L, 2.0 mmol, 2.0 equiv) and toluene (0.5 mL). The test tube was sealed and the reaction mixture was stirred at 110 °C for 38 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel, eluting with diethyl ether. The filtrate was concentrated in vacuo. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane:diethyl ether 30:1) provided 96 mg (54% yield) of the known title compound as a colorless oil.

15 **Example 175**

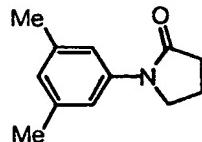
2-[(4-Methoxypheenoxy)methyl]pyridine



20 A test tube was charged with CuI (20 mg, 0.10 mmol, 0.10 equiv), 1,10-phenanthroline (36 mg, 0.20 mmol, 0.20 equiv), Cs₂CO₃ (652 mg, 2.0 mmol, 2.0 equiv), 4-iodoanisole (234 mg, 1.0 mmol, 1.0 equiv), 2-pyridylcarbinol (193 μ L, 2.0 mmol, 2.0 equiv) and toluene (0.5 mL). The test tube was sealed and the reaction mixture was stirred at 110 °C for 22 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel, eluting with diethyl ether. The filtrate was concentrated in vacuo. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane:diethyl ether 1:1) provided 120 mg (56% yield) of the title compound as a light yellow solid.

Example 1761-Bromo-2-benzyloxybenzene

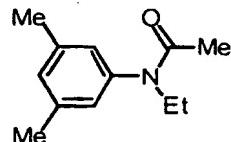
A test tube was charged with CuI (20 mg, 0.10 mmol, 0.10 equiv), 1,10-phenanthroline (36 mg, 0.20 mmol, 0.20 equiv), Cs₂CO₃ (456 mg, 1.4 mmol, 1.4 equiv), benzyl alcohol (207 µL, 2.0 mmol, 2.0 equiv), 2-bromo-iodobenzene (128 µL, 1.0 mmol, 1.0 equiv) and toluene (0.5 mL). The test tube was sealed and the reaction mixture was stirred at 110 °C for 36 h. The resulting suspension was cooled to room temperature and filtered through a 1×1 cm pad of silica gel, eluting with dichloromethane. The filtrate was concentrated in vacuo. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane:dichloromethane 2:1) provided 187 mg (71% yield) of the title compound as a colorless oil.

Example 177N-(3,5-Dimethylphenyl)-2-pyrrolidinone using potassium 4-cyano-2,6-di-*tert*-butylphenoxy as the base

A 15 mL resealable Schlenk tube was charged with CuI (9.6 mg, 0.0504 mmol, 5.0 mol%); potassium 4-cyano-2,6-di-*tert*-butylphenoxy (325 mg, 1.21 mmol), evacuated and backfilled with argon. 5-Iodo-*m*-xylene (145 µL, 1.00 mmol), 2-pyrrolidinone (94 µL, 1.24 mmol) and toluene (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 100 °C for 23 h. The resulting suspension was allowed to reach room temperature. Dodecane (internal GC standard, 230 µL) and ethyl acetate (2 mL) were added. A 0.1 mL sample of the supernatant solution was diluted with ethyl acetate (1 mL) and analyzed by GC to provide 95% yield of the desired product.

Example 178

N-(3,5-Dimethylphenyl)-N-ethylacetamide using 4-dimethylaminopyridine as ligand, sodium *tert*-butoxide as base and N-methyl-2-pyrrolidinone as solvent



5 A Schlenk tube was charged with CuI (190 mg, 1.00 mmol), 4-dimethylaminopyridine (245 mg, 2.01 mmol), sodium *tert*-butoxide (115 mg, 1.20 mmol), evacuated and backfilled with argon. 5-Iodo-*m*-xylene (145 μ L, 1.00 mmol), *N*-ethylacetamide (142 μ L, 1.51 mmol), and *N*-methyl-2-pyrrolidinone (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was
 10 stirred at 110 °C for 25 h. The resulting brown suspension was allowed to reach room temperature, poured into a solution of 30% aq ammonia (2 mL) in water (20 mL), and extracted with CH₂Cl₂ (3×15 mL). The combined organic phases were dried (Na₂SO₄) and concentrated by rotary evaporation. The residue was purified by flash chromatography on silica gel (2×15 cm; hexane-ethyl acetate 3:2; 15 mL fractions). Fractions 8-16 provided
 15 164 mg (86% yield) of the product as a white solid.

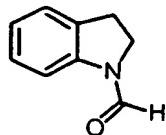
Example 179

N-(3,5-Dimethylphenyl)-N-methylformamide using bis(1-methylimidazol-2-yl)ketone as ligand

A 15 mL resealable Schlenk tube was charged with CuI (9.6 mg, 0.0504 mmol, 5.0 mol%), bis(1-methylimidazol-2-yl)ketone (19 mg, 0.100 mmol, 10 mol%), K₃PO₄ (430 mg, 2.03 mmol), evacuated and backfilled with argon. 5-Iodo-*m*-xylene (145 μ L, 1.00 mmol), *N*-methylformamide (72 μ L, 1.23 mmol) and toluene (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 110 °C for 24 h. The resulting suspension was allowed to reach room temperature. Dodecane (internal GC standard, 230 μ L) and ethyl acetate (2 mL) were added. A 0.1 mL sample of the supernatant solution was diluted with ethyl acetate (1 mL) and analyzed by GC to provide 95% yield of the desired product.

Example 180

N-Formylindoline from the corresponding aryl bromide at room temperature in 4 h using 1 equiv of water

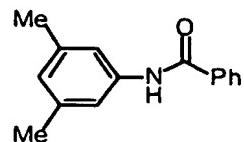


5 A Schlenk tube was charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol%), *N*-[2-(2-bromophenyl)ethyl]formamide (229 mg, 1.00 mmol), Cs₂CO₃ (500 mg, 1.53 mmol), evacuated and backfilled with argon. *N,N'*-Dimethylethylenediamine (11 µL, 0.10 mmol, 10 mol%), THF (1 mL), and finally water (18 µL, 1.0 mmol) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 25±5 °C for 4 h. The resulting pale blue-green suspension was filtered through a 0.5×1 cm pad of silica gel eluting with ethyl acetate (20 mL). The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2×10 cm; hexane-ethyl acetate 2:3; 15 mL fractions). Fractions 8-17 provided 147 mg (100% yield) of the product as a pale yellow solid.

10 °C for 4 h. The resulting pale blue-green suspension was filtered through a 0.5×1 cm pad of silica gel eluting with ethyl acetate (20 mL). The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2×10 cm; hexane-ethyl acetate 2:3; 15 mL fractions). Fractions 8-17 provided 147 mg (100% yield) of the product as a pale yellow solid.

Example 181

Preparation of *N*-(3,5-dimethylphenyl)benzamide at room temperature for 7 h using 1 equiv of water

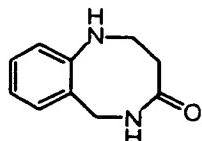


15 A Schlenk tube was charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol%), benzamide (146 mg, 1.21 mmol), Cs₂CO₃ (500 mg, 1.53 mmol), evacuated and backfilled with argon. *N,N'*-Dimethylethylenediamine (11 µL, 0.10 mmol, 10 mol%), 5-iodo-*m*-xylene (145 µL, 1.00 mmol), THF (1.0 mL), and finally water (18 µL, 1.0 mmol) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 25±5 °C for 7 h. The resulting white suspension was filtered through a 0.5×1 cm pad of silica gel eluting with ethyl acetate (20 mL). The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2×20 cm; hexane-ethyl acetate 3:1; 15

mL fractions; the sample was solubilized with 1 mL of CH₂Cl₂). Fractions 9-15 provided 223 mg (99% yield) of the product as white crystals.

Example 182

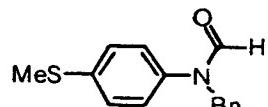
2,3,5,6-Tetrahydro-1*H*-benzo[*b*]-1,5-diazocin-4-one using tandem aryl amidation-ring expansion reaction



A Schlenk tube was charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol%), 2-azetidinone (86 mg, 1.21 mmol), K₃PO₄ (430 mg, 2.03 mmol), evacuated, and backfilled with Ar. *N,N'*-Dimethylethylenediamine (11 μL, 0.103 mmol, 10 mol%), 2-iodobenzylamine (132 μL, 1.00 mmol), and toluene (1 mL) were added under Ar. The Schlenk tube was sealed and the reaction mixture was stirred at 100 °C for 22 h. The resulting suspension was allowed to reach room temperature, poured into a solution of 30% aq ammonia (1 mL) in water (20 mL), and extracted with 3×20 mL CH₂Cl₂. The combined organic layers were dried (Na₂SO₄), concentrated, and the residue was purified by flash chromatography on silica gel (2×15 cm, ethyl acetate-methanol 10:1, 15 mL fractions). Fractions 10-20 provided 144 mg of the desired product (82% yield) as a white solid.

Example 183

N-Benzyl-*N*-(4-thiomethylphenyl)formamide



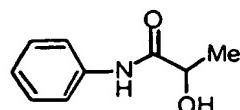
A Schlenk tube was charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol%), 4-bromothioanisole (204 mg, 1.00 mmol), *N*-benzylformamide (163 mg, 1.21 mmol), K₂CO₃ (280 mg, 2.12 mmol), briefly evacuated and backfilled with argon. *N,N'*-Dimethylethylenediamine (11 μL, 0.10 mmol, 10 mol%) and toluene (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 110 °C for 23 h. The resulting pale brown suspension was allowed to reach room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with ethyl acetate (10 mL). The filtrate was concentrated and the residue was purified by flash chromatography on

silica gel (2×15 cm; hexane-ethyl acetate 2:1; 15 mL fractions). Fractions 9-19 provided 243 mg (94% yield) of the product as a white solid. Mp: 73-74 °C.

Example 184

2-Hydroxy-N-phenylpropionamide using DMF as solvent

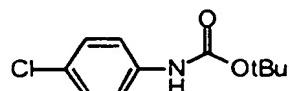
5



A Schlenk tube was charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol%), racemic lactamide (107 mg, 1.20 mmol), K₃PO₄ (430 mg, 2.03 mmol), evacuated and backfilled with argon. *N,N'*-Dimethylethylenediamine (11 µL, 0.10 mmol, 10 mol%), iodobenzene (112 µL, 1.00 mmol) and dimethylformamide (1.0 mL) were added under argon. The 10 Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 60 °C for 23 h. The resulting purple-blue suspension was allowed to reach room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with 10:1 dichloromethane-methanol (20 mL). The filtrate was concentrated using a rotary evaporation followed by evacuation at 0.1 mm Hg to remove dimethylformamide. The residue was purified by flash 15 chromatography on silica gel (2×20 cm; dichloromethane-methanol 25:1; 15 mL fractions). Fractions 10-16 provided 146 mg (88% yield) of the product as a pale tan solid.

Example 185

N-tert-Butoxycarbonyl-4-chloroaniline



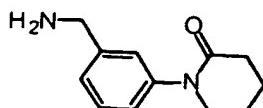
20 A Schlenk tube was charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol%), 4-bromo-1-chlorobenzene (192 mg, 1.00 mmol), *tert*-butyl carbamate (142 mg, 1.21 mmol), K₂CO₃ (280 mg, 2.03 mmol), briefly evacuated and backfilled with argon. *N,N'*-Dimethylethylenediamine (11 µL, 0.10 mmol, 10 mol%) and toluene (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 110 °C for 23 h. The resulting pale blue suspension was allowed to reach room 25 temperature and filtered through a 0.5×1 cm pad of silica gel eluting with ethyl acetate (10 mL). The filtrate was concentrated and the residue was purified by flash chromatography on

silica gel (2×20 cm; hexane-ethyl acetate 9:1; 15 mL fractions). Fractions 12-22 provided 178 mg (78% yield) of the product as white crystals.

Example 186

N-(3-Aminomethylphenyl)-2-piperidone

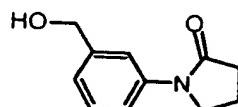
5



A Schlenk tube was charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol%), δ-valerolactam (120 mg, 1.21 mmol), K₃PO₄ (430 mg, 2.03 mmol), briefly evacuated and backfilled with argon. *N,N'*-Dimethylethylenediamine (11 μL, 0.10 mmol, 10 mol%), 3-iodobenzylamine (134 μL, 1.01 mmol), and toluene (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 100 °C for 18 h. The resulting pale yellow suspension was allowed to reach room temperature, and then 30% aq ammonia (1 mL) and water (10 mL) were added. The biphasic mixture was extracted with CH₂Cl₂ (3×15 mL). The combined organic phases were dried (Na₂SO₄), concentrated, and the residue was purified by flash chromatography on silica gel (2×15 cm; CH₂Cl₂(saturated with 30% aq ammonia)-CH₂Cl₂-MeOH 10:10:1; 15 mL fractions). Fractions 14-19 provided 199 mg (96% yield) of the product as a pale yellow oil.

Example 187

N-(3-Hydroxymethylphenyl)-2-pyrrolidinone



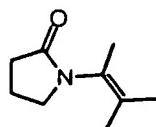
A Schlenk tube was charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol%) and K₃PO₄ (430 mg, 2.03 mmol), evacuated and backfilled with argon. *N,N'*-Dimethylethylenediamine (11 μL, 0.10 mmol, 10 mol%), 3-iodobenzyl alcohol (128 μL, 1.01 mmol), 2-pyrrolidinone (94 μL, 1.24 mmol) and toluene (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 80 °C for 3 h. The resulting white suspension was allowed to reach room temperature and filtered through a 0.5×1 cm pad of silica gel eluting with 5:1 ether-methanol (10 mL). The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2×20 cm;

dichloromethane-methanol 25:1; 15 mL fractions). Fractions 14-19 provided 180 mg (93% yield) of the product as a white solid. Mp: 120-121 °C.

Example 188

N-(3-Methyl-2-butenyl)-2-pyrrolidinone from a vinyl bromide

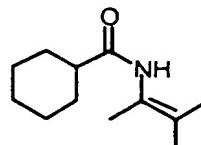
5



A 15 mL screw top test tube fitted with a PTFE septum cap was charged with CuI (10.0 mg, 0.05 mmol, 5 mol%) and K₂CO₃ (276 mg, 2.00 mmol). 2-Pyrrolidinone (76 μL, 1.00 mmol), 2-bromo-3-methyl-2-butene (116 μL, 1.00 mmol), *N,N'*-dimethyl ethylenediamine (11 μL, 0.10 mmol, 10 mol %), and 1,4-dioxane (1 mL) were added, via syringe, while purging with nitrogen. The septum cap was replaced with a solid, Teflon-lined cap and the reaction was stirred magnetically at 100 °C for 38 h. The resulting heterogeneous solution was allowed to cool before dilution with 5 mL ethyl acetate. The reaction mixture was filtered and the solution obtained was concentrated to a yellow oil. The crude material was purified by silica gel chromatography using methylene chloride : ethyl acetate (80:20); the product was isolated, as a yellow oil, in 69% yield (105.3 mg). ¹H NMR (300 MHz, CDCl₃): 1.60 (d, *J* = 1.4 Hz, 3H), 1.74 (s, 3H), 1.79 (dd, *J* = 1.3, 1.1 Hz, 3H), 2.14 (m, 2H), 2.42 (t, *J* = 8.1 Hz, 2H), 3.44 (t, *J* = 6.8 Hz, 2H). ¹³C NMR (75.5 MHz, CDCl₃): 14.9, 18.5, 19.4, 19.5, 30.9, 47.5, 124.9, 129.0, 173.2.

Example 189

N-(3-methyl-2-butenyl)benzamide from a vinyl bromide

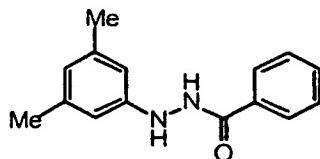


A 15 mL screw top test tube fitted with a PTFE septum cap was charged with CuI (10.0 mg, 0.05 mmol, 5 mol%), K₂CO₃ (276 mg, 2.00 mmol), and cyclohexane carboxamide (127 mg, 1.00 mmol). 2-Bromo-3-methyl-2-butene (116 μL, 1.00 mmol), *N,N'*-dimethyl ethylenediamine (11 μL, 0.10 mmol, 10.0 mol %), and 1,4-dioxane (1 mL) were added, via syringe, while purging with nitrogen. The septum cap was replaced with a solid, Teflon-lined cap and the reaction was stirred magnetically at 100 °C for 38 h. The resulting

heterogeneous solution was allowed to cool before dilution with 5 mL ethyl acetate. The reaction mixture was filtered and the solvent was removed to yield a white solid. The crude material was purified by recrystallization from ethyl acetate : hexanes (1:1); the product was obtained as white, fibrous crystals in 62 % yield (121.7 mg). ¹H NMR (300 MHz, CDCl₃): 1.55 (m, 10H), 1.60 (s, 3H), 1.68 (s, 3H), 1.87 (s, 3H), 2.12 (m, 1H), 6.40 (broad s, 1H). ¹³C NMR (75.5 MHz, CDCl₃): 17.5, 19.5, 19.7, 25.8, 29.7, 29.9, 45.7, 124.0, 124.4, 174.1.

Example 190

N'-(3,5-dimethylphenyl)benzhydrazide from an aryl bromide

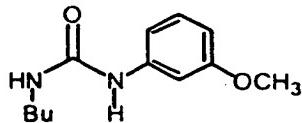


10

CuOAc (6 mg, 0.05 mmol), *N,N*-diethylsalicylamide (39 mg, 0.20 mmol), benzhydrazide (207 mg, 1.5 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). 5-Bromo-*m*-xylene (136 μL, 1.0 mmol) and DMF (0.5 mL) were added by syringes. The reaction was heated at 90 °C for 22 hours. The reaction was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 μL) were added. The organic phase was analyzed by GC or GC-MS. The reaction was further extracted by ethyl acetate (4×10 mL). The combined organic phases were washed with brine and dried over Na₂SO₄. Solvent was removed *in vacuo* and the yellow residue was purified by column chromatography on silica gel using dichloromethane/ethyl acetate (20:1) as eluent to afford the desired product as a white solid (107 mg, 46% yield). R_f = 0.5 (dichloromethane/ethyl acetate = 20:1).

Example 191

N-Butyl-N'-(3-methoxyphenyl)urea



25

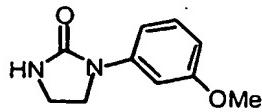
A test tube was charged with CuI (10 mg, 0.05 mmol, 0.05 equiv), K₃PO₄ (425 mg, 2.0 mmol, 2.0 equiv), butylurea (232 mg, 2.0 mmol, 2.0 equiv), filled with argon. 3-

Iodoanisole (119 μ L, 1.0 mmol, 1.0 equiv), *N,N'*-dimethylethylenediamine (11 μ L, 0.10 mmol, 0.10 equiv) and dry toluene (1.0 mL) were added under argon. The test tube was sealed and the reaction mixture was stirred at 110 °C for 24 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel, eluting with diethyl ether. The filtrate was concentrated in vacuo. Purification of the residue by flash chromatography on silica gel (2×20 cm; pentane:diethyl ether 1:2) provided 188 mg (85% yield) of the title compound as a light yellow oil.

5

Example 192***N*-(3-Methoxyphenyl)-2-imidazolidone**

10



15

A test tube was charged with CuI (40 mg, 0.20 mmol, 0.10 equiv), K₃PO₄ (850 mg, 2.0 mmol, 2.0 equiv), 2-imidazolidone (2.58 g, 30.0 mmol, 15.0 equiv), 3-iodoanisole (238 μ L, 2.0 mmol, 1.0 equiv), *N,N'*-dimethylethylenediamine (44 μ L, 0.40 mmol, 0.20 equiv) and dry DMF (4.0 mL), filled with argon. The test tube was sealed and the reaction mixture was stirred at 120 °C for 7 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel, eluting with ethyl acetate. The filtrate was concentrated in vacuo. Purification of the residue by flash chromatography on silica gel (2×20 cm; hexane:ethyl acetate 1:2) provided 288 mg (75% yield) of the title compound as a light yellow solid.

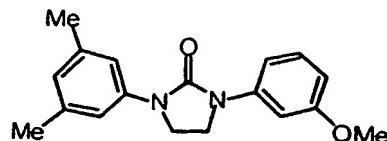
20

Example 193**Preparation of *N*-(3-methoxyphenyl)-2-imidazolidone using microwave irradiation**

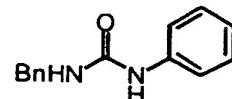
25

A microwave test tube was charged with CuI (20 mg, 0.10 mmol, 0.10 equiv), K₃PO₄ (425 mg, 2.0 mmol, 2.0 equiv), 2-imidazolidone (1.29 g, 15.0 mmol, 15.0 equiv), 3-iodoanisole (119 μ L, 1.0 mmol, 1.0 equiv), *N,N'*-dimethylethylenediamine (22 μ L, 0.20 mmol, 0.20 equiv) and dry DMF (2.0 mL), filled with argon. The test tube was sealed and the reaction mixture was stirred at 130 °C for 15 h in the microwave. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel, eluting with ethyl acetate. The filtrate was concentrated in vacuo. Purification of the residue by flash chromatography on silica gel (2×20 cm; hexane:ethyl acetate 1:2) provided 128 mg (67% yield) of the title compound as a white solid.

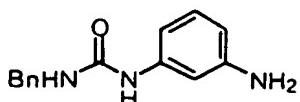
30

Example 194N-(3-Methoxyphenyl)-N'-(3,5-dimethylphenyl)-2-imidazolidone

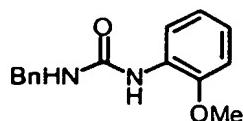
A microwave test tube was charged with CuI (20 mg, 0.10 mmol, 0.20 equiv),
 5 K₃PO₄ (212 mg, 1.0 mmol, 2.0 equiv), *N*-(3-methoxyphenyl)-2-imidazolidone (96 mg, 0.5
 mmol, 1.0 equiv), 3,5-dimethyliodobenzene (144 µL, 1.0 mmol, 2.0 equiv), *N,N'*-
 dimethylethylenediamine (22 µL, 0.20 mmol, 0.40 equiv) and dry DMF (2.0 mL), filled with
 argon. The test tube was sealed and the reaction mixture was stirred at 130 °C for 15 h and
 at 160 °C for further 15 h in the microwave. The resulting suspension was cooled to room
 10 temperature and filtered through a 0.5×1 cm pad of silica gel, eluting with ethyl acetate.
 The filtrate was concentrated in vacuo. Purification of the residue by flash chromatography
 on silica gel (2×20 cm; hexane:ethyl acetate 4:1) provided 134 mg (91% yield) of the title
 compound as a white solid.

Example 195*N*-Benzyl-*N'*-phenyl-urea

A test tube was charged with CuI (20 mg, 0.10 mmol, 0.10 equiv), K₃PO₄ (425 mg,
 2.0 mmol, 2.0 equiv), benzylurea (225 mg, 1.5 mmol, 1.5 equiv), filled with argon.
 Bromobenzene (105 µL, 1.0 mmol, 1.0 equiv), *N,N'*-dimethylethylenediamine (22 µL, 0.20
 20 mmol, 0.20 equiv) and dry dioxane (1.0 mL) were added under argon. The test tube was
 sealed and the reaction mixture was stirred at 80 °C for 25 h. The resulting suspension was
 cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel, eluting with
 ethyl acetate. The filtrate was concentrated in vacuo. The solid residue was dissolved in ~2
 mL DMF. Purification of the residue by flash chromatography on silica gel (2×20 cm;
 25 hexane:ethyl acetate 3:1) provided 179 mg (79% yield) of the title compound as a white
 solid.

Example 196**N-Benzyl-N'-(3-aminophenyl)urea**

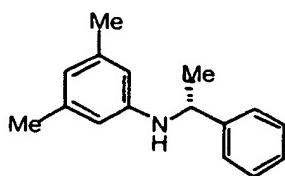
A test tube was charged with CuI (20 mg, 0.10 mmol, 0.10 equiv), K₃PO₄ (425 mg, 5 2.0 mmol, 2.0 equiv), benzylurea (225 mg, 1.5 mmol, 1.5 equiv), 3-bromoaniline (109 µL, 1.0 mmol, 1.0 equiv), *N,N'*-dimethylethylendiamine (22 µL, 0.20 mmol, 0.20 equiv) and dry dioxane (1.0 mL), filled with nitrogen. The test tube was sealed and the reaction mixture was stirred at 80 °C for 24 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel, eluting with ethyl acetate. The filtrate was 10 concentrated in vacuo. The solid residue was dissolved in ~2 mL DMF. Purification of the residue by flash chromatography on silica gel (2×20 cm; hexane:ethyl acetate 1:2) provided 185 mg (77% yield) of the title compound as a light yellow solid.

Example 197**N-Benzyl-N'-(2-methoxyphenyl)urea**

15 A test tube was charged with CuI (20 mg, 0.10 mmol, 0.10 equiv), K₃PO₄ (425 mg, 2.0 mmol, 2.0 equiv), benzylurea (225 mg, 1.5 mmol, 1.5 equiv), 2-bromoanisole (125 µL, 1.0 mmol, 1.0 equiv), *N,N'*-dimethylethylendiamine (22 µL, 0.20 mmol, 0.20 equiv) and dry dioxane (1.0 mL), filled with nitrogen. The test tube was sealed and the reaction mixture was stirred at 80 °C for 26 h. The resulting suspension was cooled to room temperature and filtered through a 0.5×1 cm pad of silica gel, eluting with ethyl acetate. The filtrate was concentrated in vacuo. The solid residue was dissolved in ~2 mL DMF. Purification of the residue by flash chromatography on silica gel (2×20 cm; hexane:ethyl acetate 2:1) provided 172 mg (67% yield) of the title compound as a white solid.

20 **Example 198**

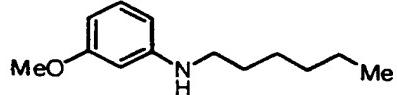
(R)-N-(3,5-dimethylphenyl)-α-methylbenzylamine



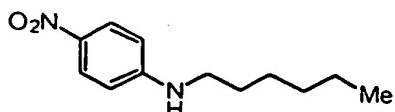
CuOAc (6 mg, 0.05 mmol), *N,N*-diethylsalicylamide (39 mg, 0.20 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). 5-Bromo-*m*-xylene (136 5 μL, 1.0 mmol), (*R*)-α-methylbenzylamine (193 μL, 1.5 mmol) and DMF (0.5 mL) were added by syringes. The reaction mixture was stirred at 100 °C for 30 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 μL) were added. The organic phase was analyzed by GC or GC-MS. The reaction mixture was further extracted by ethyl 10 acetate (4×10 mL). The combined organic phases were washed with brine and dried over Na₂SO₄. Solvent was removed *in vacuo* and the yellow residue was purified by column chromatography on silica gel using hexane/ethyl acetate (20:1) as eluent to afford the desired product as a colorless oil (160 mg, 71% yield, 98% ee). R_f = 0.4 (hexane/ethyl acetate = 20:1). HPLC conditions: (column: Daciell OD; flow rate: 0.7 mL/min; UV lamp: 15 254 nm; solvent system: hexane/2-propanol (9:1); retention time: 7.80 min).

Example 199

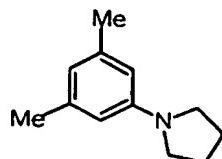
3-Methoxy-N-hexylaniline from 3-chloroanisole



CuOAc (6 mg, 0.05 mmol), *N,N*-diethylsalicylamide (39 mg, 0.20 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). 3-Chloroanisole (122 20 μL, 1.0 mmol) and *n*-hexylamine (0.5 mL, as solvent) were added by syringes. The reaction mixture was stirred at 130 °C for 24 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 μL) were added. The organic phase was analyzed by GC which afforded 25 64% conversion of 3-chloroanisole and 40% GC yield of the desired product.

Example 200**4-Nitro-N-hexylaniline from 1-chloro-4-nitrobenzene**

CuOAc (6 mg, 0.05 mmol), *N,N*-diethylsalicylamide (39 mg, 0.20 mmol), 1-chloro-5 4-nitrobenzene (158 mg, 1.0 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). *n*-Hexylamine (198 μL, 1.5 mmol) and DMF (0.5 mL) were added by syringes. The reaction mixture was stirred at 120 °C for 22 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), 10 ammonium hydroxide (~0.5 mL) and dodecane (227 μL) were added. The organic phase was analyzed by GC and GC-MS. The reaction mixture was further extracted by ethyl acetate (4×10 mL). The combined organic phases were washed with brine and dried over Na₂SO₄. Solvent was removed *in vacuo* and the orange residue was purified by column chromatography on silica gel using hexane/ethyl acetate (10:1) as eluent to afford the 15 desired product as a yellow solid (199 mg, 90% yield). R_f = 0.2 (hexane/ethyl acetate = 10:1).

Example 201***N*-(3,5-Dimethylphenyl)pyrrolidine with DMF as solvent**

20 Cul (10 mg, 0.05 mmol), *N,N*-diethylsalicylamide (39 mg, 0.20 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). 5-Bromo-*m*-xylene (136 μL, 1.0 mmol), pyrrolidine (333 μL, 4.0 mmol) and DMF (0.5 mL) were added by syringes. The reaction mixture was stirred at 100 °C for 20 h. The reaction mixture was allowed to 25 reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 μL) were added. The organic phase was analyzed by GC and

GC-MS. A 99% conversion of 5-bromo-*m*-xylene and 74% calibrated GC yield was obtained.

Example 202

N-(3,5-Dimethylphenyl)pyrrolidine in neat pyrrolidine

5 CuI (10 mg, 0.05 mmol), *N,N*-diethylsalicylamide (39 mg, 0.20 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). 5-Bromo-*m*-xylene (136 µL, 1.0 mmol) and pyrrolidine (250 µL, 3.0 mmol) were added by syringes. The reaction mixture was stirred at 100 °C for 20 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 µL) were added. The organic phase was analyzed by GC and GC-MS. A 86% conversion of 5-bromo-*m*-xylene and 65% calibrated GC yield was obtained.

10

10 CuI (10 mg, 0.05 mmol), *N,N*-diethylsalicylamide (39 mg, 0.20 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). 5-Bromo-*m*-xylene (136 µL, 1.0 mmol) and pyrrolidine (250 µL, 3.0 mmol) were added by syringes. The reaction mixture was stirred at 100 °C for 20 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 µL) were added. The organic phase was analyzed by GC and GC-MS. A 86% conversion of 5-bromo-*m*-xylene and 65% calibrated GC yield was obtained.

Example 203

N-(4-Chlorophenyl)piperidine

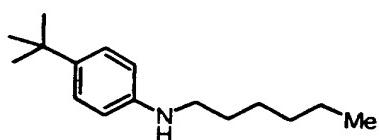


CuI (10 mg, 0.05 mmol), *N,N*-diethylsalicylamide (39 mg, 0.20 mmol), 4-bromochlorobenzene (191 mg, 1.0 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). Piperidine (148 µL, 1.5 mmol) and DMF (0.5 mL) were added by syringes. The reaction mixture was stirred at 90 °C for 20 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 µL) were added. The organic phase was analyzed by GC and GC-MS. A 75% conversion of 4-bromochlorobenzene and 29% calibrated GC yield was obtained.

20

25 **Example 204**

4-*tert*-Butyl-N-hexylaniline from 4-*tert*-butylphenyl trifluoromethanesulfonate



CuI (10 mg, 0.05 mmol), *N,N*-diethylsalicylamide (39 mg, 0.20 mmol) and Na₂CO₃ (127 mg, 1.2 mmol) were put into a screw-capped test tube with a Teflon-lined septum.

The tube was then evacuated and backfilled with argon (3 cycles). 4-*tert*-Butylphenyl trifluoromethanesulfonate (282 mg, 1.0 mmol), *n*-hexylamine (198 μ L, 1.5 mmol) and DMF (0.5 mL) were added by syringes. The reaction mixture was stirred at 90 °C for 18 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 μ L) were added. The organic phase was analyzed by GC and GC-MS. A 3% calibrated GC yield was obtained.

Example 205

Evaluation of Various Copper Catalysts in the Cu-Catalyzed Amination of an Aryl Bromide in DMF (See Figure 5)

Copper complex (0.05 mmol), *N,N*-diethylsalicylamide (39 mg, 0.2 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). 5-Bromo-*m*-xylene (136 μ L, 1.0 mmol), *n*-hexylamine (198 μ L, 1.5 mmol) and DMF (0.5 mL) were added by syringes. The reaction mixture was stirred at 70 °C for 24 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 μ L) were added. The organic phase was analyzed by GC or GC-MS. The results are presented in Figure 5.

Example 206

Evaluation of Various Solvents in the Cu-catalyzed Amination of an Aryl Bromide (See Figure 6)

Copper(I) iodide (10 mg, 0.05 mmol), *N,N*-diethylsalicylamide (39 mg, 0.2 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). 5-Bromo-*m*-xylene (136 μ L, 1.0 mmol), *n*-hexylamine (198 μ L, 1.5 mmol) and solvent (0.5 mL) were added by syringes. The reaction mixture was stirred at 100 °C for 18 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 μ L) were added. The organic phase was analyzed by GC or GC-MS. The results are presented in Figure 6.

Example 207

Evaluation of Various Ligands in the Cu-Catalyzed Amination of Aryl Bromides in DMF (See Figure 7)

CuI (10-19 mg, 0.05-0.10 mmol), ligand (0.2 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). Aryl bromide (1.0 mmol), *n*-hexylamine (198 μL, 1.5 mmol) and DMF (0.5 mL) were added by syringes. The reaction mixture was stirred at 100 °C for 20 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 μL) were added. The organic phase was analyzed by GC or GC-MS. The results are presented in Figure 7.

Example 208

- 10 **Evaluation of Various Ligands in the Cu-catalyzed Amination of an Aryl Bromide without Solvent (See Figure 8)**

CuI (10 mg, 0.05 mmol), ligand (0.2 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). 5-Bromo-*m*-xylene (136 μL, 1.0 mmol), *n*-hexylamine (198 μL, 1.5 mmol) were added by syringes. The resulting mixture was stirred at 100 °C for 18 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 μL) were added. The organic phase was analyzed by GC or GC-MS. The results are presented in Figure 8.

Example 209

- 20 **Evaluation of the Cu-catalyzed Amination of an Aryl Bromide in DMF using Low Catalyst Loading (See Figure 9)**

CuI (2-10 mg, 0.01-0.05 mmol), *N,N*-diethylsalicylamide (10-39 mg, 0.05-0.20 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). 5-Bromo-*m*-xylene (136 μL, 1.0 mmol), *n*-hexylamine (198 μL, 1.5 mmol) and DMF (0.5 mL) were added by syringes. The resulting mixture was stirred at 90-100 °C for 18-54 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 μL) were added. The organic phase was analyzed by GC or GC-MS. The results are presented in Figure 9.

- 30 **Example 210**

Cu-Catalyzed Amination of Functionalized Aryl Bromides (See Figure 10)

CuI (10 mg, 0.05 mmol), *N,N*-diethylsalicylamide (39 mg, 0.20 mmol), aryl bromide (if solid; 1.0 mmol), and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). Aryl bromide (if liquid; 1.0 mmol), amine (1.5 mmol), and DMF (0.5 mL) were added by syringes. The reaction mixture was stirred at 90 °C for 18-22 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 µL) were added. The organic phase was analyzed by GC or GC-MS. The reaction mixture was further extracted by ethyl acetate (4×10 mL). The combined organic phases were washed with brine and dried over Na₂SO₄. Solvent was removed in *vacuo* and the residue was purified by column chromatography on silica gel to afford the desired product.

N-Hexyl-3,5-dimethylaniline (Figure 10, entry 1)

Using the general procedure, 5-bromo-*m*-xylene (136 µL, 1.0 mmol) was coupled with *n*-hexylamine (198 µL, 1.5 mmol). Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (20:1) as eluent afforded the desired product as a colorless oil (187 mg, 91% yield).

3-Amino-N-hexylaniline (Figure 10, entry 2)

Using the general procedure, 3-bromoaniline (172 mg, 1.0 mmol) was coupled with *n*-hexylamine (198 µL, 1.5 mmol). Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (2:1) as eluent afforded the desired product as a colorless oil (154 mg, 80% yield). R_f = 0.4 (hexane/ethyl acetate = 2:1).

4-(N-(3,5-Dimethylphenyl)amino)butanol (Figure 10, entry 3)

Using the general procedure, 5-bromo-*m*-xylene (136 µL, 1.0 mmol) was coupled with 4-aminobutanol (138 µL, 1.5 mmol). Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (2:1) as eluent afforded the desired product as a colorless oil (174 mg, 90% yield). R_f = 0.4 (hexane/ethyl acetate = 1:1).

4-Methyl-N-(2-(1-cyclohexenyl)ethyl)aniline (Figure 10, entry 4)

Using the general procedure, 4-bromotoluene (172 mg, 1.0 mmol) was coupled with 2-(1-cyclohexenyl)ethylamine (209 µL, 1.5 mmol). Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (20:1) as eluent afforded the desired product as a colorless oil (205 mg, 95% yield). R_f = 0.6 (hexane/ethyl acetate = 10:1).

4-(N-Benzyl)aminothioanisole (Figure 10, entry 5)

Using the general procedure, 4-bromothioanisole (203 mg, 1.0 mmol) was coupled with benzylamine (164 μ L, 1.5 mmol). Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (15:1) as eluent afforded the desired product as a white solid (201 mg, 88% yield). $R_f = 0.4$ (hexane/ethyl acetate = 10:1).

2-(4-(N-Benzyl)amino)phenoxyethanol (Figure 10, entry 6)

Using the general procedure, 2-(4-bromophenoxy)ethanol (217 mg, 1.0 mmol) was coupled with benzylamine (164 μ L, 1.5 mmol). Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (2:1) as eluent afforded the desired product as a colorless oil (201 mg, 84% yield). $R_f = 0.5$ (hexane/ethyl acetate = 1:1).

3,4-(Methylenedioxy)-N-furfurylaniline (Figure 10, entry 7)

Using the general procedure, 4-bromo-1,2-(methylenedioxy)benzene (120 μ L, 1.0 mmol) was coupled with furfurylamine (132 μ L, 1.5 mmol). Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (8:1) as eluent afforded the desired product as a colorless oil (187 mg, 87% yield). $R_f = 0.5$ (hexane/ethyl acetate = 5:1).

4-(N-Hexyl)aminobenzonitrile (Figure 10, entry 8)

Using the general procedure, 4-bromobenzonitrile (182 mg, 1.0 mmol) was coupled with *n*-hexylamine (198 μ L, 1.5 mmol). Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (6:1) as eluent afforded the desired product as a light yellow solid (145 mg, 72% yield). $R_f = 0.6$ (hexane/ethyl acetate = 3:1).

4-(N-(2-Methoxy)ethyl)aminoacetophenone (Figure 10, entry 9)

Using the general procedure, 4-bromoacetophenone (199 mg, 1.0 mmol) was coupled with 2-methoxyethylamine (130 μ L, 1.5 mmol). Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (1:1) as eluent afforded the desired product as a light yellow solid (148 mg, 77% yield). $R_f = 0.6$ (hexane/ethyl acetate = 2:3).

3-Nitro-N-hexylaniline (Figure 10, entry 10)

Using the general procedure, 3-bromonitrobenzene (202 mg, 1.0 mmol) was coupled with *n*-hexylamine (198 μ L, 1.5 mmol). Purification of the crude product by column

chromatography on silica gel using hexane/ethyl acetate (6:1) as eluent afforded the desired product as a light yellow solid (174 mg, 78% yield). $R_f = 0.5$ (hexane/ethyl acetate = 5:1).

4-(*N*-(4-Chlorophenyl))aminomethylpiperidine (Figure 10, entry 11)

Using the general procedure, 4-bromochlorobenzene (192 mg, 1.0 mmol) was coupled with 4-aminomethylpiperidine (171 mg, 1.5 mmol). Purification of the crude product by column chromatography on silica gel using methanol/dichloromethane (saturated with ammonia) (1:20) as eluent afforded the desired product as a light yellow solid (138 mg, 62% yield). $R_f = 0.3$ (methanol/dichloromethane (saturated with ammonia) (1:20)).

Example 211

10 **Cu-Catalyzed Amination of *ortho*-Substituted, Dibromo-Substituted and Heterocyclic Aryl Bromides (See Figure 11)**

CuI (10 mg, 0.05 mmol), *N,N*-diethylsalicylamide (39 mg, 0.20 mmol), aryl bromide (if solid; 1.0 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). Aryl bromide (if liquid; 1.0 mmol), amine (1.2-4.0 mmol) and DMF (0.5 mL) were added by syringes. The reaction mixture was stirred at 90-100 °C for 18-24 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 µL) were added. The organic phase was analyzed by GC or GC-MS. The reaction mixture was further extracted by ethyl acetate (4×10 mL). The combined organic phases were washed with brine and dried over Na₂SO₄. Solvent was removed in *vacuo* and the yellow residue was purified by column chromatography on silica gel to afford the desired product.

2-Methoxy-*N*-hexylaniline (Figure 11, entry 1)

Using the general procedure, 2-bromoanisole (125 µL, 1.0 mmol) was coupled with *n*-hexylamine (198 µL, 1.5 mmol) at 100 °C for 22 h. Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (30:1) as eluent afforded the desired product as a colorless liquid (184 mg, 89% yield). $R_f = 0.4$ (hexane/ethyl acetate = 20:1).

2-(*N*-Hexylamino)benzylalcohol (Figure 11, entry 2)

30 Using the general procedure, 2-bromobenzyl alcohol (187 mg, 1.0 mmol) was coupled with *n*-hexylamine (198 µL, 1.5 mmol) at 90 °C for 22 h. Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (6:1) as eluent

afforded the desired product as a colorless liquid (168 mg, 81% yield). $R_f = 0.7$ (hexane/ethyl acetate = 2:1).

2-(N-2-(1-Cyclohexenyl)ethyl)amino-para-xylene (Figure 11, entry 3)

Using the general procedure, 2-bromo-*p*-xylene (138 μ L, 1.0 mmol) was coupled 5 with 2-(1-cyclohexenyl)ethylamine (209 μ L, 1.5 mmol) at 100 °C for 24 h. Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (30:1) as eluent afforded the desired product as a colorless oil (180 mg, 79% yield). $R_f = 0.5$ (hexane/ethyl acetate = 20:1).

4-Bromo-N-hexylaniline (Figure 11, entry 4)

10 Using the general procedure, 1,4-dibromobenzene (236 mg, 1.0 mmol) was coupled with *n*-hexylamine (158 μ L, 1.2 mmol) at 90 °C for 20 h. Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (20:1) as eluent afforded the desired product as a colorless oil (212 mg, 83% yield). $R_f = 0.6$ (hexane/ethyl acetate = 10:1).

15 *N,N'-Dihexyl-4-aminoaniline (Figure 11, entry 5)*

CuI (10 mg, 0.05 mmol), *N,N*-diethylsalicylamide (39 mg, 0.20 mmol), 1,4-dibromobenzene (236 mg, 1.0 mmol) and K₃PO₄ (636 mg, 3.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). *n*-Hexylamine (527 μ L, 4.0 mmol) and DMF (0.5 mL) 20 were added by syringes. The reaction mixture was stirred at 100 °C for 42 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 μ L) were added. The organic phase was analyzed by GC or GC-MS. The reaction mixture was further extracted by ethyl acetate (4×10 mL). The combined organic phases were washed with brine and dried over 25 Na₂SO₄. Solvent was removed in *vacuo* and the brown residue was purified by column chromatography on silica gel using hexane/ethyl acetate (5:1) as eluent to afford the desired product as a brown solid (224 mg, 81% yield). $R_f = 0.3$ (hexane/ethyl acetate = 5:1).

3-(N-(3-Pyridyl)aminomethyl)pyridine (Figure 11, entry 6)

Using the general procedure, 3-bromopyridine (96 μ L, 1.0 mmol) was coupled with 30 3-(aminomethyl)pyridine (153 μ L, 1.5 mmol) at 90 °C for 20 h. Purification of the crude product by column chromatography on silica gel using dichloromethane(saturated with ammonia)/methanol (15:1) as eluent afforded the desired product as a light yellow liquid.

(153 mg, 83% yield). $R_f = 0.4$ (dichloromethane(saturated with ammonia)/methanol = 10:1).

3-(N-(2-(1-Cyclohexenyl)ethyl))aminothianaphthene (Figure 11, entry 7)

Using the general procedure, 3-bromothianaphthene (131 μ L, 1.0 mmol) was coupled with 2-(1-cyclohexenyl)ethylamine (209 μ L, 1.5 mmol) at 90 °C for 20 h. Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (20:1) as eluent afforded the desired product as a deep yellow liquid (211 mg, 82% yield). $R_f = 0.4$ (hexane/ethyl acetate = 20:1).

5-(N-(4-Methoxybenzyl))aminopyrimidine (Figure 11, entry 8)

Using the general procedure, 5-bromopyrimidine (159 mg, 1.0 mmol) was coupled with 4-methoxybenzylamine (196 μ L, 1.5 mmol) at 90 °C for 22 h. Purification of the crude product by column chromatography on silica gel using dichloromethane(saturated with ammonia)/ethyl acetate (1:1) as eluent afforded the desired product as a white solid (183 mg, 85% yield). $R_f = 0.2$ (dichloromethane(saturated with ammonia)/ethyl acetate = 1:1).

Example 212

Cu-Catalyzed Amination of Functionalized Aryl Bromides without Solvent (See Figure 12)

CuI (10 mg, 0.05 mmol), *N,N*-diethylsalicylamide (10 mg, 0.05 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum.

The tube was then evacuated and backfilled with argon (3 cycles). Aryl bromide (1.0 mmol) and amine (1.5 mmol) were added by syringes. The mixture was stirred at 90-100 °C for 18-22 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 μ L) were added. The organic phase was analyzed by GC or GC-MS. The reaction mixture was further extracted by ethyl acetate (4×10 mL). The combined organic phases were washed with brine and dried over Na₂SO₄. Solvent was removed in *vacuo* and the residue was purified by column chromatography on silica gel to afford the desired product.

N-Hexyl-3,5-dimethylaniline (Figure 12, entry 1)

Using the general procedure, 5-bromo-*m*-xylene (136 μ L, 1.0 mmol) was coupled with *n*-hexylamine (198 μ L, 1.5 mmol). Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (20:1) as eluent afforded the desired product as a colorless oil (185 mg, 90% yield).

N-(4-Methylphenyl)-3,5-dimethylaniline (Figure 12, entry 2)

CuI (10 mg, 0.05 mmol), *N,N*-diethylsalicylamide (10 mg, 0.05 mmol), 4-toluidine (161, 1.5 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). 5-Bromo-*m*-xylene (136 μL, 1.0 mmol) was added by a syringe. The reaction mixture was stirred at 100 °C for 20 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 μL) were added. The organic phase was analyzed by GC and 22% conversion of 5-bromo-*m*-xylene and 9% GC yield of the desired product was obtained.

10 *N-(3,5-Dimethylphenyl)indole (Figure 12, entry 3)*

CuI (10 mg, 0.05 mmol), *N,N*-diethylsalicylamide (10 mg, 0.05 mmol), indole (176 mg, 1.5 mmol) and K₃PO₄ (425 mg, 2.0 mmol) were put into a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). 5-Bromo-*m*-xylene (136 μL, 1.0 mmol) was added by a syringe. The reaction mixture was stirred at 100 °C for 20 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 μL) were added. The organic phase was analyzed by GC or GC-MS. The reaction mixture was further extracted by ethyl acetate (4×10 mL). The combined organic phases were washed with brine and dried over Na₂SO₄. Solvent was removed in *vacuo* and the yellow residue was purified by column chromatography on silica gel using hexane/ethyl acetate (10:1) as eluent to afford the desired product as a brown solid (196 mg, 89% yield).

3-Nitro-N-hexylaniline (Figure 12, entry 4)

Using the general procedure, 3-bromonitrobenzene (202 mg, 1.0 mmol) was coupled with *n*-hexylamine (198 μL, 1.5 mmol) at 100 °C for 22 h. Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (6:1) as eluent afforded the desired product as a light yellow solid (132 mg, 59% yield). R_f = 0.5 (hexane/ethyl acetate = 5:1).

3-Amino-N-hexylaniline (Figure 12, entry 5)

Using the general procedure, 3-bromoaniline (172 mg, 1.0 mmol) was coupled with *n*-hexylamine (198 μL, 1.5 mmol) at 100 °C for 20 h. Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (2:1) as eluent afforded the

desired product as a colorless oil (137 mg, 71% yield). $R_f = 0.4$ (hexane/ethyl acetate = 2:1).

4-Methyl-N-(2-(1-cyclohexenyl)ethyl)aniline (Figure 12, entry 6)

Using the general procedure, 4-bromotoluene (172 mg, 1.0 mmol) was coupled with 5 2-(1-cyclohexenyl)ethylamine (209 μ L, 1.5 mmol) at 100 °C for 20 h. Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (20:1) as eluent afforded the desired product as a colorless oil (198 mg, 92% yield). $R_f = 0.6$ (hexane/ethyl acetate = 10:1).

4-(N-(4-Chlorophenyl))aminomethylpiperidine (Figure 12, entry 7)

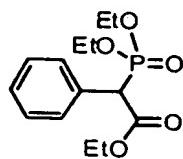
10 Using the general procedure, 4-bromochlorobenzene (192 mg, 1.0 mmol) was coupled with 4-aminomethylpiperidine (171 mg, 1.5 mmol) at 100 °C for 20 h. Purification of the crude product by column chromatography on silica gel using methanol/dichloromethane (saturated with ammonia) (1:20) as eluent afforded the desired product as a light yellow solid (134 mg, 60% yield). $R_f = 0.3$ (methanol/dichloromethane 15 (saturated with ammonia) = 1:20).

3-(N-Hexyl)aminopyridine (Figure 12, entry 8)

Using the general procedure, 3-bromopyridine (96 μ L, 1.0 mmol) was coupled with *n*-hexylamine (198 μ L, 1.5 mmol) at 90 °C for 18 h. Purification of the crude product by column chromatography on silica gel using hexane/ethyl acetate (1:1) as eluent afforded the 20 desired product as a colorless oil (146 mg, 82% yield). $R_f = 0.2$ (hexane/ethyl acetate = 2:1).

Example 213

C-Arylation of Triethyl phosphonoacetate



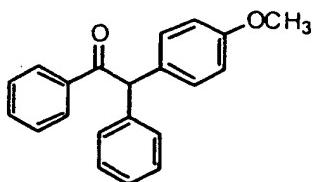
25 *Procedure Using Iodobenzene*

An oven dried Schlenk tube equipped with a magnetic stirbar and a Teflon stopcock was evacuated while hot and cooled under argon. The tube was charged with CuI (9.8 mg, 5.1 mol %) and Cs₂CO₃ (0.434 g, 1.33 mmol). The tube was evacuated and backfilled with argon (3 times), and the Teflon stopcock was replaced with a rubber septum. *Trans*-1,2-

- diaminocyclohexane (12 μ L, 10.0 mol %) was added volumetrically, followed by iodobenzene (114 μ L, 1.00 mmol), triethyl phosphonoacetate (220 μ L, 1.11 mmol), and anhydrous toluene (1.0 mL). The septum was replaced by the Teflon stopcock under a positive pressure of argon, and the sealed tube was placed in an oil bath preheated to 70 °C.
- 5 After 22 h, the reaction was allowed to cool to room temperature, and was partitioned between ethyl acetate (20 mL) and saturated aqueous NH₄Cl (10 mL). The organic portion was dried (Na₂SO₄) and filtered through Celite. The solution was then analyzed by gas chromatography, which indicated complete conversion of iodobenzene to the above compound in 93% GC yield.
- 10 *Procedure Using Bromobenzene*
- An oven dried Schlenk tube equipped with a magnetic stirbar and a Teflon stopcock was evacuated while hot and cooled under argon. The tube was charged with CuI (9.5 mg, 5.0 mol %) and Cs₂CO₃ (0.428 g, 1.31 mmol). The tube was evacuated and backfilled with argon (3 times), and the Teflon stopcock was replaced with a rubber septum. *Trans*-1,2-diaminocyclohexane (12 μ L, 10.0 mol %) was added volumetrically, followed by bromobenzene (109 μ L, 1.00 mmol), triethyl phosphonoacetate (220 μ L, 1.11 mmol), and anhydrous toluene (1.0 mL). The septum was replaced by the Teflon stopcock under a positive pressure of argon, and the sealed tube was placed in an oil bath preheated to 70 °C.
- 15 After 16.5 h, the reaction was allowed to cool to room temperature, and was partitioned between ethyl acetate (20 mL) and saturated aqueous NH₄Cl (10 mL). The organic portion was dried (Na₂SO₄) and filtered through Celite. The solution was then analyzed by gas chromatography, which indicated complete conversion of bromobenzene to the above compound in 2% GC yield.
- 20

Example 214

25 C-Arylation of Deoxybenzoin



An oven dried Schlenk tube equipped with a magnetic stirbar and a Teflon stopcock was evacuated while hot and cooled under argon. The tube was charged with CuI (9.4 mg,

4.9 mol%), K₃PO₄ (0.435 g, 2.05 mmol), 4-iodoanisole (0.235 g, 1.00 mmol), and deoxybenzoin (0.295 g, 1.46 mmol). The tube was evacuated and backfilled with argon (3 times), and the Teflon stopcock was replaced with a rubber septum. *Trans*-1,2-diaminocyclohexane (12 µL, 10.0 mol%) was added volumetrically, followed by anhydrous toluene (1.0 mL). The septum was replaced by the Teflon stopcock under a positive pressure of argon, and the sealed tube was placed in an oil bath preheated to 110 °C. After 42 h, the reaction was allowed to cool to room temperature, and was partitioned between ethyl acetate (20 mL) and saturated aqueous NH₄Cl (10 mL). The organic portion was dried (Na₂SO₄), filtered through Celite, and concentrated via rotary evaporation. The oil thus obtained was purified by silica gel chromatography to give the product shown as a pale yellow oil (64 mg, 21%).

Example 215

Benzonitrile from iodobenzene and copper cyanide using N,N'-dimethylethylenediamine as ligand

A Schlenk tube was charged with CuCN (108 mg, 1.21 mmol), evacuated, backfilled with Ar. *N,N'*-Dimethylethylenediamine (21.5 µL, 0.202 mmol, 20 mol%), iodobenzene (112 µL, 1.00 mmol), and toluene (1.0 mL) were added under Ar. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 110 °C for 17 h. Dodecane (internal GC standard, 230 µL) and ethyl acetate (2 mL) were added. A 0.1 mL sample of the supernatant solution was diluted with ethyl acetate (1 mL) and analyzed by GC to provide a 31% yield of benzonitrile.

Example 216

3,5-Dimethylbenzonitrile from 5-bromo-*m*-xylene and potassium cyanide using N,N'-dimethylethylenediamine as ligand

A Schlenk tube was charged with CuI (19.5 mg, 0.102 mmol, 20 mol%), KCN (78 mg, 1.20 mmol), evacuated, backfilled with Ar. *N,N'*-Dimethylethylenediamine (21.5 µL, 0.202 mmol, 20 mol%), 5-bromo-*m*-xylene (136 µL, 1.00 mmol), and toluene (1.0 mL) were added under Ar. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 110 °C for 24 h. Dodecane (internal GC standard, 230 µL), ethyl acetate (2 mL), and 30% aq ammonia (1 mL) were added. A 0.1 mL sample of the

supernatant solution was diluted with ethyl acetate (1 mL) and analyzed by GC to provide a 15% yield of 3,5-dimethylbenzonitrile.

Example 217

Cu-Catalyzed arylation of indole in dioxane with 4-bromotoluene and various ligands
5 **(Figure 13)**

To a flame-dried resealable test tube was added CuI (1 mol%), indole (1.2 mmol) and K₃PO₄ (2.1 mmol). The test tube was fixed with a rubber septum, was evacuated and back-filled with argon, and this evacuation/back-fill procedure was repeated. To this tube 4-bromotoluene (1.0 mmol), the ligand (10 mol%), dodecane (0.20 mmol, internal GC standard) and dioxane (1 mL) were then added successively under argon. The reaction tube was sealed using a screw cap and the contents were stirred with heating via an oil bath at 110 C for 24 hours. The reaction mixture was cooled to ambient temperature, diluted with 2-3 mL ethyl acetate, and filtered through a plug of silica gel, eluting with 10-20 mL of ethyl acetate. The filtrate was analyzed by GC and compared to a known sample of authentic product to provide a corrected GC yield (Figure 13).

Example 218

Cu-Catalyzed arylation of indole in toluene with 4-bromotoluene and various ligands
(Figure 14)

The procedure outlined in Example 217 was used, with toluene (1 mL) as the solvent. The ligands depicted in Figure 14 were used. Corrected GC yields are shown in Figure 14.

Example 219

Cu-Catalyzed arylation of indole in toluene with 2-bromotoluene and various ligands
(Figures 15 and 16)

To a flame-dried resealable test tube was added CuI (1 mol%), indole (1.0 mmol) and K₃PO₄ (2.1 mmol). The test tube was fixed with a rubber septum, was evacuated and back-filled with argon, and this evacuation/back-fill procedure was repeated. To this tube 2-bromotoluene (1.0 mmol), the ligand (20 mol%, Figure 15 or 16), dodecane (0.20 mmol, internal GC standard) and toluene (1 mL) were then added successively under argon. The reaction tube was sealed using a screw cap and the contents were stirred with heating via an oil bath at 110 C for 24 hours. The reaction mixture was cooled to ambient temperature, diluted with 2-3 mL ethyl acetate, and filtered through a plug of silica gel, eluting with 10-

20 mL of ethyl acetate. The filtrate was analyzed by GC and compared to a known sample of authentic product to provide a corrected GC yield (shown in Figures 15 and 16).

Example 220

Arylation of acetamide generated *in situ* from *N,O*-bis(trimethylsilyl)acetamide

5 A Schlenk tube was charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol %), KF (350 mg, 6.0 mmol), evacuated, backfilled with Ar. *N,N'*-Dimethylethylenediamine (11 μ L, 0.10 mmol, 10 mol%), 2-iodotoluene (128 μ L, 1.01 mmol), *N,O*-bis(trimethylsilyl)acetamide (300 μ L, 1.21 mmol), and toluene (1.0 mL) were added under Ar. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 110 °C for 16 h. The 10 resulting suspension was allowed to reach room temperature and then filtered through a 0.5×1 cm pad of silica gel eluting with ethyl acetate (20 mL). The filtrate was concentrated and the residue was purified by flash chromatography on silica gel (2×15 cm; hexane-ethyl acetate 1:4; 15 mL fractions). Fractions 10-17 provided 78 mg (52% yield) of *N*-(2-methylphenyl)acetamide as white needles.

15 **Example 221**

Arylation of *N*-phenyl acetamide using copper(II) acetylacetone or copper(II) 2,2,6,6-tetramethyl-3,5-heptadienoate as the catalyst

A Schlenk tube was charged with Cu(II) acetylacetone (14 mg, 0.054 mmol, 5.1 mol %), *N*-phenylacetamide (165 mg, 1.22 mmol), Cs₂CO₃ (460 mg, 1.41 mmol), 20 evacuated, backfilled with Ar. In a separate flask, a stock solution of 5-iodo-*m*-xylene (3.0 mL) and dodecane (internal GC standard, 4.7 mL) in dioxane (20 mL) was prepared. A portion of the stock solution (1.4 mL) containing 1.05 mmol of 5-iodo-*m*-xylene was added to the Schlenk tube under Ar. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 110 °C for 22 h. The resulting white suspension was 25 allowed to reach room temperature. A 0.1 mL sample of the suspension was filtered through a plug of Celite eluting with ethyl acetate (1 mL). The filtrate was analyzed by GC to provide a 58% yield of the desired product.

Use of copper(II) 2,2,6,6-tetramethyl-3,5-heptadienoate (23 mg, 0.054 mmol, 5.1 mol%) in place of Cu(II) acetylacetone and the reaction was performed at 110 °C for 24 h, 30 GC analysis indicated a 68% yield of *N*-(3,5-dimethylphenyl)-*N*-phenylacetamide.

Example 222**Arylation of N-phenylacetamide using various ligands (Figure 17)**

A Schlenk tube was charged with CuI (10 mg, 0.053 mmol, 5.0 mol %), the ligand (in those cases where the ligand was a solid) *N*-phenylacetamide (165 mg, 1.22 mmol),
5 Cs₂CO₃ (460 mg, 1.41 mmol), evacuated, backfilled with Ar. The ligand (in those cases where the ligand was a liquid), 5-iodo-*m*-xylene (150 µL, 1.04 mmol), dodecane (internal GC standard, 235 µL), and dioxane (1.0 mL) were added under Ar. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 110 °C for 23 h. The resulting suspension was allowed to reach room temperature. A 0.1 mL sample of the
10 suspension was filtered through a plug of Celite eluting with ethyl acetate (1 mL), and the filtrate was analyzed by GC. The results are presented in Figure 17.

Example 223**Arylation of 2-pyrrolidinone with 5-iodo-*m*-xylene using various 1,2-diamine ligands (Figure 18)**

15 A Schlenk tube was charged with CuI (10 mg, 0.052 mmol, 5.0 mol %), K₃PO₄ (450 mg, 2.1 mmol), evacuated, backfilled with Ar. Ligand (0.11 mmol, 10 mol%), 5-iodo-*m*-xylene (150 µL, 1.04 mmol), 2-pyrrolidinone (94 µL, 1.24 mmol), and toluene (1.0 mL) were added under Ar. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 60 °C for 4 h. The resulting suspension was allowed to reach room
20 temperature. Dodecane (internal GC standard, 235 µL) and ethyl acetate (1 mL) were added. A 0.1 mL sample of the supernatant solution was diluted with ethyl acetate (1 mL) and analyzed by GC. The results are presented in Figure 18.

Example 224**Arylation of N-benzylformamide with 5-bromo-*m*-xylene using various 1,2-diamine ligands (Figure 19)**

Ten 15 mL test tubes with screw threads were equipped with one 10×3 mm Teflon-coated stirring bar each and charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol%) and K₂CO₃ (280 mg, 2.03 mmol). Each test tube was closed with an open-top screw cap fitted with a Teflon-lined silicon rubber septum, evacuated through a 21-gauge needle, and then
30 backfilled with argon. Meanwhile, a stock solution of 5-bromo-*m*-xylene (2.04 mL, 15.0 mmol), *N*-benzylformamide (2.44 g, 18.1 mmol), and dodecane (internal GC standard, 0.68 mL) in toluene (15 mL) was prepared in a 25 mL pear-shaped flask under argon. To each

test tube were added 1.28 mL of the stock solution followed by the ligand using syringes. The reaction mixtures in the test tubes were stirred in a 110 ± 5 °C oil bath for 22 h. The test tubes were then allowed to reach room temperature, the screw caps were removed, and ethyl acetate (2 mL) was added. A 50-100 μ L sample of the supernatant solution from each test 5 tube was diluted with ethyl acetate (1 mL) and the resulting solutions were analyzed by GC. The results are presented in Figure 19.

Example 225

Arylation of *N*-methylformamide using various ligands (Figure 20)

Six 15 mL test tubes with screw threads were equipped with one 10 \times 3 mm Teflon-coated stirring bar each and charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol%), the ligand (in those cases where the ligand was a solid; 0.10 mmol), and K₃PO₄ (430 mg, 2.03 mmol). Each test tube was closed with an open-top screw cap fitted with a Teflon-lined silicon rubber septum, evacuated through a 21-gauge needle, and then backfilled with argon. Meanwhile, a stock solution of 5-iodo-*m*-xylene (2.16 mL, 15.0 mmol), *N*- 10 methylformamide (1.06 mL, 18.1 mmol), and dodecane (internal GC standard, 0.68 mL) in toluene (15 mL) was prepared in a 25 mL pear-shaped flask under argon. To each test tube was added 1.28 mL of the stock solution containing 1.0 mmol of 5-iodo-*m*-xylene and 1.2 mmol of *N*-methylformamide, using a syringe followed by the ligand (in those cases where the ligand was a liquid; 0.10 mmol). The top of the septum was then covered with a dab of 15 vacuum grease to seal the injection spot. The reaction mixtures in the test tubes were stirred in a 110 ± 5 °C oil bath for 24 h. The test tubes were then allowed to reach room 20 temperature, the screw caps were removed, and ethyl acetate (3 mL) was added. A 50-100 μ L sample of the supernatant solution from each test tube was diluted with ethyl acetate (1 mL) and the resulting solutions were analyzed by GC. The results are reported in Figure 20.

Example 226

Arylation of *N*-methylformamide using di-*tert*-butylphosphine oxide as the ligand

A Schlenk tube was charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol%), di-*tert*-butylphosphine oxide (16.5 mg, 0.102 mmol), K₃PO₄ (430 mg, 2.03 mmol), evacuated, backfilled with Ar. 5-Iodo-*m*-xylene (145 μ L, 1.00 mmol), *N*-methylformamide (72 μ L, 30 1.23 mmol), and toluene (1.0 mL) were added under Ar. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 110 °C for 24 h. The suspension was

allowed to reach room temperature. Dodecane (internal GC standard, 230 μ L) and ethyl acetate (2 mL) were added. A 0.1 mL sample of the supernatant solution was diluted with ethyl acetate (1 mL) and analyzed by GC to provide a 46% yield of *N*-(3,5-dimethylphenyl)-*N*-methylformamide.

5 **Example 227**

Arylation of *N*-methylformamide using hexamethylphosphorous triamide as the ligand

A Schlenk tube was charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol%), K₃PO₄ (430 mg, 2.03 mmol), evacuated, backfilled with Ar. Hexamethylphosphorous triamide (18.5 μ L, 0.102 mmol, 10 mol%) 5-iodo-*m*-xylene (145 μ L, 1.00 mmol), *N*-methylformamide (72 μ L, 1.23 mmol), and toluene (1.0 mL) were added under Ar. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 110 °C for 24 h. The suspension was allowed to reach room temperature. Dodecane (internal GC standard, 230 μ L) and ethyl acetate (2 mL) were added. A 0.1 mL sample of the supernatant solution was diluted with ethyl acetate (1 mL) and analyzed by GC to provide 76% yield of *N*-(3,5-dimethylphenyl)-*N*-methylformamide.

15 *N*-methylformamide.

Example 228

Arylation of *N*-methylformamide using 3,1'-dimethyl-4,5-dihydro-3H,1'H-[1,2']biimidazolyl-2-one as the ligand

A Schlenk tube was charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol%), 3,1'-dimethyl-4,5-dihydro-3H,1'H-[1,2']biimidazolyl-2-one (18 mg, 0.10 mmol, 10 mol%), K₃PO₄ (430 mg, 2.03 mmol), evacuated, backfilled with Ar. 5-Iodo-*m*-xylene (145 μ L, 1.00 mmol), *N*-methylformamide (72 μ L, 1.23 mmol), and toluene (1.0 mL) were added under Ar. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 110 °C for 24 h. The suspension was allowed to reach room temperature. Dodecane (internal GC standard, 230 μ L) and ethyl acetate (2 mL) were added. A 0.1 mL sample of the supernatant solution was diluted with ethyl acetate (1 mL) and analyzed by GC to provide 54% yield of *N*-(3,5-dimethylphenyl)-*N*-methylformamide.

Example 229

Arylation of *N*-methylformamide using various copper sources (Figure 21)

30 Nine 15 mL test tubes with screw threads were equipped with one 10×3 mm Teflon-coated stirring bar each and charged with K₃PO₄ (430 mg, 2.03 mmol) and one of the

following copper sources: 1) copper powder, bronze (Aldrich, 99%; 3.2 mg, 0.050 mmol); 2) CuI (Strem, 98%; 9.6 mg, 0.050 mmol); 3) CuCl (Strem, 97+%; 5.0 mg, 0.050 mmol); 4) CuSCN (Aldrich, 98+%; 6.1 mg, 0.050 mmol); 5) Cu₂O (Alfa Aesar, 99%; 3.6 mg, 0.025 mmol); 6) CuCl₂ (Strem, 98%; 6.8 mg, 0.051 mmol); 7) CuSO₄·5H₂O (Aldrich, 98+%; 5 12.5 mg, 0.0501 mmol); 8) Cu(OAc)₂ (Strem, 99%; 9.1 mg, 0.050 mmol); 9) Cu(II) acetylacetone (Lancaster, 98%; 13.1 mg, 0.0500 mmol). Each test tube was closed with an open-top screw cap fitted with a Teflon-lined silicon rubber septum, evacuated through a 21-gauge needle, and then backfilled with argon. Meanwhile, a stock solution of 5-iodo-*m*-xylene (2.16 mL, 15.0 mmol), *N*-methylformamide (1.06 mL, 18.1 mmol), *N,N'*-dimethylethylenediamine (160 µL, 1.50 mmol) and dodecane (internal GC standard, 0.68 mL) in toluene (15 mL) was prepared in a 25 mL pear-shaped flask under argon. To each test tube was added 1.28 mL of the stock solution containing 1.0 mmol of 5-iodo-*m*-xylene, 1.2 mmol of *N*-methylformamide, 0.10 mmol of *N,N'*-dimethylethylenediamine using a syringe. The top of the septum was then covered with a dab of vacuum grease to seal the 10 injection spot. The reaction mixtures in the test tubes were stirred in a 80±5 °C oil bath for 7 h. The test tubes were then allowed to reach room temperature, the screw caps were removed, and ethyl acetate (2 mL) was added. A 50-100 µL sample of the supernatant solution from each test tube was diluted with ethyl acetate (1 mL) and the resulting 15 solutions were analyzed by GC. The results are reported in Figure 21.

20 **Example 230**

Arylation of *N*-methyl-4-methylbenzenesulfonamide using various bases (Figure 22)

A Schlenk tube was charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol %), the base (2.0-4.1 mmol), evacuated, backfilled with Ar (in the case of *N,N,N',N'*-tetramethylguanidine as the base, it was added after the Schlenk tube was backfilled with 25 Ar). *N,N'*-Dimethylethylenediamine (11 µL, 0.10 mmol, 10 mol%), iodobenzene (112 µL, 1.00 mmol), and toluene (1.0 mL) were added under Ar. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 110 °C for 22 h. The resulting suspension was allowed to reach room temperature. Dodecane (internal GC standard, 230 µL) and ethyl acetate (3 mL) were added. A 0.1 mL sample of the supernatant solution was 30 diluted with ethyl acetate (1 mL) and analyzed by GC. The results are presented in Figure 22.

Example 231Arylation of 2-pyrrolidinone using potassium triphosphate as the base

A test tube with a screw thread was equipped with a 10×3 mm Teflon-coated stirring bar and charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol%) and K₅P₃O₁₀ (Strem, finely ground, 430 mg, 0.96 mmol). The test tube was closed with an open-top screw cap fitted with a Teflon-lined silicon rubber septum, evacuated through a 21-gauge needle, and then backfilled with argon. Meanwhile, a stock solution of 5-iodo-*m*-xylene (2.16 mL), 2-pyrrolidinone (1.40 mL), and dodecane (internal GC standard, 0.68 mL) in toluene (15 mL) was prepared in a 25 mL pear-shaped flask under argon. A portion of the stock solution (1.28 mL) containing 1.0 mmol of 5-iodo-*m*-xylene and 1.2 mmol of 2-pyrrolidinone was added using a syringe, followed by *N*-methylethylenediamine (8.9 μL, 1.0 mmol, 10 mol%). The reaction mixture in the test tube was stirred in a 60±5 °C oil bath for 5 h. The test tube was then allowed to reach room temperature, the screw cap was removed, and ethyl acetate (2 mL) was added. A 50-100 μL sample of the supernatant solution from the test tube was diluted with ethyl acetate (1 mL). GC analysis of the resulting solution indicated a 95% yield of *N*-(3,5-dimethylphenyl)-2-pyrrolidinone.

- Use of *N,N'*-dimethylethylenediamine (11 μL, 1.0 mmol, 10 mol%) in place of *N*-methylethylenediamine provided a 93% yield of *N*-(3,5-dimethylphenyl)-2-pyrrolidinone according to GC analysis.
- Use of ethylenediamine (6.8 μL, 1.0 mmol, 10 mol%) in place of *N*-methylethylenediamine provided a 61% yield of *N*-(3,5-dimethylphenyl)-2-pyrrolidinone according to the GC analysis.

Example 232Arylation of *n*-hexyl amine using various bases (Figure 23)

- CuI (10 mg, 0.05 mmol), base (2.0 mmol) and *N,N*-diethylsalicylamide (39 mg, 0.2 mmol) were added to a screw-capped test tube equipped with Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). 5-Bromo-*m*-xylene (136 μL, 1.0 mmol), *n*-hexylamine (198 μL, 1.5 mmol) and DMF (0.5 mL) were added by syringes. The reaction mixture was stirred and heated at 90 °C for 18 hours. The test tube was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium

hydroxide (~0.5 mL) and dodecane (227 μ L) were added. The organic phase was analyzed by GC. The results are presented in Figure 23.

Example 233

Arylation of benzylamine using various bases (Figure 24)

5 CuI (19 mg, 0.1 mmol) and base (2.0 mmol) were added to a screw-capped test tube equipped with a Teflon-lined septum. The test tube was evacuated and backfilled with argon (3 cycles). 2-Propanol (1.0 mL), ethylene glycol (111 μ L, 2.0 mmol), iodobenzene (112 μ L, 1.0 mmol) and benzylamine (131 μ L, 1.2 mmol) were added by syringes. The reaction mixture was stirred and heated at 80 °C for 18 hours. The reaction mixture was
10 allowed to reach room temperature. Diethyl ether (~2 mL), water (~10 mL) and dodecane (227 μ L) were added. The organic phase was analyzed by GC. The results are presented in Figure 24.

Example 234

Arylation of benzylamine using various diols as ligands (Figure 25)

15 CuI (19 mg, 0.1 mmol) and anhydrous K₃PO₄ (425 mg, 2.0 mmol) were added to a screw-capped test tube equipped with a Teflon-lined septum. The test tube was evacuated and backfilled with argon (3 cycles). 2-Propanol (1.0 mL, not necessary if diol was used as solvent), diol (0.1-2.0 mmol), Iodobenzene (112 μ L, 1.0 mmol) and benzylamine (131 μ L, 1.2 mmol) were added by syringes. The reaction mixture was stirred and heated at 80 °C
20 for 18 hours. The reaction mixture was allowed to reach room temperature. Diethyl ether (~2 mL), water (~10 mL) and dodecane (227 μ L) were added. The organic phase was analyzed by GC. The results are presented in Figure 25.

Example 235

Arylation of benzylamine generated *in situ* from N-benzyl-trifluoroacetamide

25 A Schlenk tube was charged with CuI (9.6 mg, 0.050 mmol, 5.0 mol %), N-benzyl-trifluoroacetamide (244 mg, 1.20 mmol), K₃PO₄ (640 mg, 3.01 mmol), evacuated,
backfilled with Ar. Iodobenzene (112 μ L, 1.00 mmol), ethylene glycol (0.11 mL, 2.0 mmol), and isopropanol (1.5 mL) were added under Ar. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 80 °C for 24 h. The resulting white
30 suspension was allowed to reach room temperature. Dodecane (internal GC standard, 230 μ L), ethyl acetate (2 mL), and 30% aq ammonia (2 mL) were added. A 0.1 mL sample of

the top layer was diluted with ethyl acetate (1 mL) and analyzed by GC to provide a 76% yield of *N*-phenylbenzylamine.

Example 236

Arylation of n-hexyl amine using various ligands (Figure 26)

5 Eight test tubes with screw threads were brought into a nitrogen filled glovebox and capped, then removed from the glovebox. Copper iodide (9.5 mg, 0.050 mmol, 5.0 mol%), the ligand (in those cases where the ligand was a solid), and K₃PO₄ (440 mg, 2.07 mmol) were added to the test tubes in the air. The test tubes were immediately capped and brought into a nitrogen-filled glovebox, the caps being removed immediately before the evacuation
10 of the antechamber. Inside the glovebox, the test tubes were capped with open-top screw caps lined with a silicon rubber septum and then removed from the glovebox. In a separate flask, a stock solution of bromobenzene (1.05 mL) and *n*-hexylamine (1.60 mL) in *n*-butanol (10 mL) was prepared. The ligand (in those cases where the ligand was a liquid) and a portion of the stock solution (1.3 mL) containing 1.0 mmol of bromobenzene and 1.2
15 mmol of *n*-hexylamine were added using syringes. The open-top screw caps were replaced with solid screw caps. The reaction mixtures were stirred at 100 °C for 23 h and then allowed to reach room temperature. Dodecane (internal GC standard, 230 µL), ethyl acetate (2 mL), and water (1 mL) were added. A 0.1 mL sample of the top (organic) layer was diluted with ethyl acetate (1 mL) and analyzed by GC. The results are presented in Figure
20 26.

Incorporation by Reference

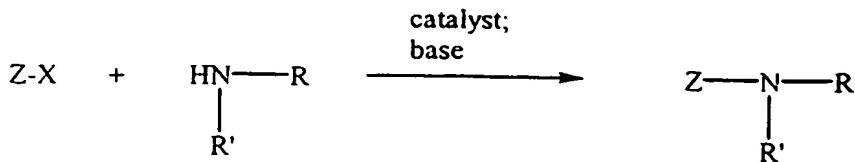
All of the patents and publications cited in the Specification are hereby incorporated by reference.

Equivalents

25 Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

We Claim:

1. A method represented by Scheme 1:



Scheme 1

wherein

- 5 X represents I, Br, Cl, alkylsulfonate, or arylsulfonate;
- Z represents optionally substituted aryl, heteroaryl or alkenyl;
- catalyst comprises a copper atom or ion, and a ligand;
- base represents a Bronsted base;
- R represents alkyl, cycloalkyl, aralkyl, aryl, heteroaryl, formyl, acyl, alkylO₂C-,
- 10 aryI O₂C-, heteroaryl O₂C-, aralkyl O₂C-, heteroaralkyl O₂C-, acyl(R')N-, alkylOC(O)N(R')-,
- arylOC(O)N(R')-, aralkylOC(O)N(R')-, heteroaralkylOC(O)N(R')-, -N=C(alkyl)₂, or -
- N=C(aryl)₂;
- R' represents H, alkyl, cycloalkyl, aralkyl, heteroaralkyl, aryl, heteroaryl, formyl,
- acyl, amino, or -C(NR")N(R")₂;
- 15 R" represents independently for each occurrence H, alkyl, cycloalkyl, aryl,
- heteroaryl, aralkyl or heteroaralkyl;
- R and R' taken together may represent =C(alkyl)₂, or =C(aryl)₂; and
- R and R' are optionally connected by a covalent bond;
- provided that when R is aryl or heteroaryl, R' is not formyl or acyl;
- 20 further provided that when R is formyl or acyl, R' is not aryl or heteroaryl.
2. The method of claim 1, wherein X represents I.
3. The method of claim 1, wherein X represents Br.
4. The method of claim 1, wherein X represents Cl.
5. The method of claim 1, wherein the ligand comprised by the catalyst is an optionally
- 25 substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium
- carbene, pyridine, or 1,10-phenanthroline.
6. The method of claim 1, wherein the ligand comprised by the catalyst is an optionally
- substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

7. The method of claim 1, wherein the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.
- 5 8. The method of claim 1, wherein the ligand comprised by the catalyst is a chelating ligand.
- 10 9. The method of claim 1, wherein the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.
- 15 10. The method of claim 1, wherein the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane; ethanolamine; 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.
- 20 11. The method of claim 1, wherein the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.
- 25 12. The method of claim 1, wherein the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
13. The method of claim 1, wherein the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 30 14. The method of claim 1, wherein the catalyst is present in less than or equal to about 10 mol% relative to Z-X.

15. The method of claim 1, wherein the catalyst is present in less than or equal to about 5 mol% relative to Z-X.
16. The method of claim 1, wherein the catalyst is present in less than or equal to about 1 mol% relative to Z-X.
- 5 17. The method of claim 1, wherein the catalyst is present in less than or equal to about 0.1 mol% relative to Z-X.
18. The method of claim 1, wherein the method is conducted at a temperature less than about 150 C.
19. The method of claim 1, wherein the method is conducted at a temperature less than 10 about 140 C.
20. The method of claim 1, wherein the method is conducted at a temperature less than about 110 C.
21. The method of claim 1, wherein the method is conducted at a temperature less than about 100 C.
- 15 22. The method of claim 1, wherein the method is conducted at a temperature less than about 90 C.
23. The method of claim 1, wherein the method is conducted at a temperature less than about 50 C.
24. The method of claim 1, wherein the method is conducted at a temperature less than 20 about 40 C.
25. The method of claim 1, wherein the method is conducted at ambient temperature.
26. The method of claim 1, wherein Z represents optionally substituted aryl.
27. The method of claim 1, wherein Z represents optionally substituted phenyl.
28. The method of claim 1, wherein R' represents H, or alkyl.
- 25 29. The method of claim 1, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.
30. The method of claim 1, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.
- 30 31. The method of claim 1, wherein X represents I; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-

(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-

5 (dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

32. The method of claim 1, wherein X represents I; and the ligand comprised by the catalyst is a chelating ligand.

33. The method of claim 1, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-

10 hydroxyethyl amine, or 1,2-diaminoethane.

34. The method of claim 1, wherein X represents I; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

35. The method of claim 1, wherein X represents I; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

36. The method of claim 1, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

37. The method of claim 1, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

38. The method of claim 1, wherein X represents I; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 5 10
39. The method of claim 1, wherein X represents I; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
40. The method of claim 1, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 15 20
41. The method of claim 1, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 25 30
42. The method of claim 1, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate,

phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

43. The method of claim 1, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

44. The method of claim 1, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

45. The method of claim 1, wherein X represents I; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

46. The method of claim 1, wherein X represents I; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

47. The method of claim 1, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethylamine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

48. The method of claim 1, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-

diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or 5 sodium hydroxide.

49. The method of claim 1, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium 10 phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

50. The method of claim 1, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

51. The method of claim 1, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

52. The method of claim 1, wherein X represents Br; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

53. The method of claim 1, wherein X represents Br; and the ligand comprised by the catalyst is a chelating ligand.

54. The method of claim 1, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

55. The method of claim 1, wherein X represents Br; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and

- trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane,
5 ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.
56. The method of claim 1, wherein X represents Br; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-
10 diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.
57. The method of claim 1, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide,
15 fluoride, or guanidine.
58. The method of claim 1, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 20 59. The method of claim 1, wherein X represents Br; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline,
25 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 30 60. The method of claim 1, wherein X represents Br; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

61. The method of claim 1, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 5 62. The method of claim 1, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 10 63. The method of claim 1, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 15 64. The method of claim 1, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or
- 20 guanidine.
65. The method of claim 1, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 25 66. The method of claim 1, wherein X represents Br; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-

- (dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
67. The method of claim 1, wherein X represents Br; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 10 68. The method of claim 1, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 15 69. The method of claim 1, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 20 70. The method of claim 1, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 25 30

71. The method of claim 1, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.
72. The method of claim 1, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.
73. The method of claim 1, wherein X represents Cl; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.
74. The method of claim 1, wherein X represents Cl; and the ligand comprised by the catalyst is a chelating ligand.
75. The method of claim 1, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.
76. The method of claim 1, wherein X represents Cl; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.
77. The method of claim 1, wherein X represents Cl; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.
78. The method of claim 1, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-

aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

79. The method of claim 1, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

80. The method of claim 1, wherein X represents Cl; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

81. The method of claim 1, wherein X represents Cl; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

82. The method of claim 1, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

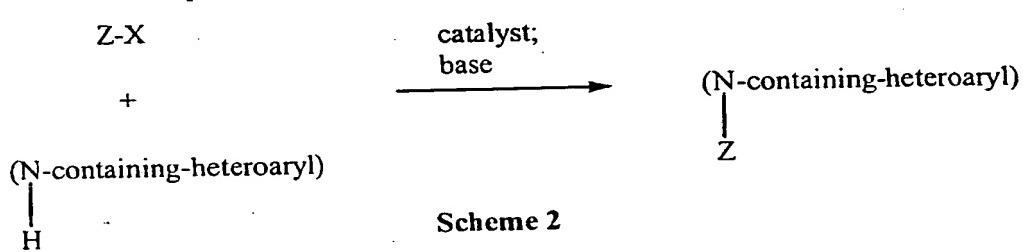
83. The method of claim 1, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a

carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

84. The method of claim 1, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 10 85. The method of claim 1, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 15 86. The method of claim 1, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
87. The method of claim 1, wherein X represents Cl; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 30 88. The method of claim 1, wherein X represents Cl; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

89. The method of claim 1, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 5 90. The method of claim 1, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 10 91. The method of claim 1, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

20 92. A method represented by Scheme 2:



wherein

X represents I, Br, Cl, alkylsulfonate, or arylsulfonate;

25 Z represents optionally substituted aryl, heteroaryl or alkenyl;

(N-containing-heteroaryl)-H represents optionally substituted pyrazole, pyrrole, tetrazole, imidazole, indazole, 1,2,3-triazole, 1,2,4-trizole, indole, carbazole, benzotriazole, benzimidazole, guanine, purine, adenine, xanthine, 8-azaadenine, 8-azoapoxanthine, uracil,

- 6-azauracil, cytocine, thymine, 6-azathymine, uric acid, benzoylene urea, 4-(3*H*)-pyrimidone, pyridone, 1(2*H*)-phthalazinone, 1,2,3-benzotriazine-4(3*H*)-one, benzimidazolinone, 2-benzoxazolinone, thymidine, uridine, (-)-inosine, 1*H*-1,2,3,5-diazadiphosphole, 1*H*-1,2,3-azadiphosphole, 1*H*-1,2,4-azadiphosphole, 1*H*-1,2,4-
- 5 diazaphosphole, 1*H*-1,2,3-diazaphosphole, 1*H*-1,3,2-diazaphosphole, 1*H*-1,2-azadiphosphole, 1*H*-1,3-azadiphosphole, 1*H*-1,2,3,4-triazaphosphole, 1*H*-1,2,3,5-dithiadiazolidene, 1*H*-1,3,2,4-dithiadiazolidene, 1,3,2-oxathiazole, 3*H*-1,2,3-oxathiazole, 1,3,2-dithiazole, 1*H*-1,2-azaborole, pentazole, 3*H*-1,2,3-dioxazole, 2*H*-1,2,3-oxadiazine, 2*H*-1,2,4-oxadiazine, 2*H*-1,2,5-oxadiazine, 2*H*-1,2,6-oxadiazine, 2*H*-1,2,3-thiadiazine, 2*H*-
- 10 1,2,4-thiadiazine, 2*H*-1,2,5-thiadiazine, 2*H*-1,2,6-thiadiazine, 2*H*-1,2-thiazine, 1,3,5,2,4,6-trithiatriazine, 2*H*-1,2,4,5-oxatriazine, 4*H*-1,3,2,4-dithiadiazine, 2*H*, 4*H*-1,3,2,5-dioxadiazine, 2*H*-1,5,2,4-dioxadiazine, 2*H*-1,2,4,6-thiatriazine, 2*H*-1,2,4,5-thiatriazine, 4*H*-1,3,2-dithiazane, 4*H*-1,3,2-dioxazine, 2*H*-1,5,2-dioxazine, 1,3,4-dithiazane, 4*H*-1,3,2-oxathiazine, 2*H*, 4*H*-1,3,2-oxathiazine, 2*H*, 4*H*-1,3,2-oxathiazine, 2*H*, 4*H*-1,2,5-oxadiazine, 2*H*-1,2,4-triazepine, 2*H*-1,3-
- 15 diazepine, 2*H*-1,4-diazepine, 2*H*-1,2,5-triazepine, 2*H*-1,3,5-triazepine, 2*H*-1,2,4-triazepine, 1*H*-azepine, 2*H*-1,2,3,5-tetrazepine, 2*H*-1,2,4,6-tetrazepine, 2*H*-1,2,4,5-tetrazepine, 2*H*-1,5,2,4-dithiadiazepine, 1,3,5,2,4,7-trithiatriazepine, 1,3,5,2,4-trithiadiazepine, pentahydro-1,3,5,2,4,6,8-trithiatetrazocine, 2*H*, 6*H*-1,5,2,4,6,8-dithiatetrazocine, 2*H*-1,2,5-oxadiazocine, 2*H*-1,2,6-oxadiazocine, 2*H*-1,2-oxazocine, 2*H*-1,2-thiazocine, 4*H*-1,2,5-thiadiazocine, 4*H*-
- 20 1,2,6-thiadiazocine, 5*H*-[1,2,4]-thiadiazolo[1,5-b][1,2,4]oxathiazole, triazolothiadiazole, thienothiadiazole, 1*H*-imidazo[1,2-a]imidazole, 4*H*-furo[3,2-b]pyrrole[3,4-b], 1*H*-pyrrolopyrazole, 1*H*-[2,3-d]thienopyrazole, 1*H*-[3,4-d]thienopyrazole, 1*H*-[2,3-c]thienopyrazole, 1*H*-[3,4-c]thienopyrazole, 1*H*-1,3-benzazaphole, 1*H*-benzazepine, 2*H*-2-benzazepine, 1*H*-1,3-benzodiazepine, 1*H*-1,4-benzodiazepine, 1*H*-1,5-benzodiazepine, 1*H*-
- 25 1,2,4-benzotriazepine, 1*H*-1,2,5-benzotriazepine, 1*H*-1,3,4-benzotriazepine, or 3*H*-3-benzazepine;
- catalyst comprises a copper atom or ion, and a ligand; and base represents a Bronsted base.
93. The method of claim 92, wherein X represents I.
- 30 94. The method of claim 92, wherein X represents Br.
95. The method of claim 92, wherein X represents Cl.

96. The method of claim 92, wherein the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.
97. The method of claim 92, wherein the ligand comprised by the catalyst is an 5 optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.
98. The method of claim 92, wherein the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.
99. The method of claim 92, wherein the ligand comprised by the catalyst is a chelating 15 ligand.
100. The method of claim 92, wherein the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.
101. The method of claim 92, wherein the ligand comprised by the catalyst is cis-1,2- 20 diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'- 25 dimethyl-1,2-diaminoethane.
102. The method of claim 92, wherein the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or 30 N,N'-dimethyl-1,2-diaminoethane.
103. The method of claim 92, wherein the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

104. The method of claim 92, wherein the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
105. The method of claim 92, wherein the catalyst is present in less than or equal to about 10 mol% relative to Z-X.
- 5 106. The method of claim 92, wherein the catalyst is present in less than or equal to about 5 mol% relative to Z-X.
107. The method of claim 92, wherein the catalyst is present in less than or equal to about 1 mol% relative to Z-X.
108. The method of claim 92, wherein the catalyst is present in less than or equal to about 10 0.1 mol% relative to Z-X.
109. The method of claim 92, wherein the method is conducted at a temperature less than about 150 C.
110. The method of claim 92, wherein the method is conducted at a temperature less than about 140 C.
- 15 111. The method of claim 92, wherein the method is conducted at a temperature less than about 110 C.
112. The method of claim 92, wherein the method is conducted at a temperature less than about 100 C.
113. The method of claim 92, wherein the method is conducted at a temperature less than 20 about 90 C.
114. The method of claim 92, wherein the method is conducted at a temperature less than about 50 C.
115. The method of claim 92, wherein the method is conducted at a temperature less than about 40 C.
- 25 116. The method of claim 92, wherein the method is conducted at ambient temperature.
117. The method of claim 92, wherein Z represents optionally substituted aryl.
118. The method of claim 92, wherein Z represents optionally substituted phenyl.
119. The method of claim 92, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.
- 30 120. The method of claim 92, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

121. The method of claim 92, wherein X represents I; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.
- 5 122. The method of claim 92, wherein X represents I; and the ligand comprised by the catalyst is a chelating ligand.
- 10 123. The method of claim 92, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.
- 15 124. The method of claim 92, wherein X represents I; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, 20 ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.
- 25 125. The method of claim 92, wherein X represents I; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.
- 30 126. The method of claim 92, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
127. The method of claim 92, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane;

and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

128. The method of claim 92, wherein X represents I; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
129. The method of claim 92, wherein X represents I; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
130. The method of claim 92, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
131. The method of claim 92, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
132. The method of claim 92, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-

diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

133. The method of claim 92, wherein X represents I; the ligand comprised by the
5 catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

134. The method of claim 92, wherein X represents I; the ligand comprised by the
10 catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

135. The method of claim 92, wherein X represents I; the ligand comprised by the
catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-
15 isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-
20 (dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

136. The method of claim 92, wherein X represents I; the ligand comprised by the
catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate,
25 cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

137. The method of claim 92, wherein X represents I; the ligand comprised by the
catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

30 138. The method of claim 92, wherein X represents I; the ligand comprised by the
catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and
trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-

dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is 5 potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

139. The method of claim 92, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-10-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

140. The method of claim 92, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

141. The method of claim 92, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

142. The method of claim 92, wherein X represents Br; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

143. The method of claim 92, wherein X represents Br; and the ligand comprised by the catalyst is a chelating ligand.

144. The method of claim 92, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

145. The method of claim 92, wherein X represents Br; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.
- 5
146. The method of claim 92, wherein X represents Br; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.
- 10
147. The method of claim 92, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 15
148. The method of claim 92, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
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149. The method of claim 92, wherein X represents Br; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
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150. The method of claim 92, wherein X represents Br; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
151. The method of claim 92, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
152. The method of claim 92, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
153. The method of claim 92, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
154. The method of claim 92, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
155. The method of claim 92, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

156. The method of claim 92, wherein X represents Br; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
157. The method of claim 92, wherein X represents Br; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
158. The method of claim 92, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
159. The method of claim 92, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
160. The method of claim 92, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium

phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

161. The method of claim 92, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.
- 5 162. The method of claim 92, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.
163. The method of claim 92, wherein X represents Cl; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-
10 isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.
- 15 164. The method of claim 92, wherein X represents Cl; and the ligand comprised by the catalyst is a chelating ligand.
165. The method of claim 92, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.
- 20 166. The method of claim 92, wherein X represents Cl; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-
25 diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.
167. The method of claim 92, wherein X represents Cl; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and
30 trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

168. The method of claim 92, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, 5 fluoride, or guanidine.
169. The method of claim 92, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 10 170. The method of claim 92, wherein X represents Cl; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline,
- 15 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 20 171. The method of claim 92, wherein X represents Cl; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
172. The method of claim 92, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 25 173. The method of claim 92, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane,

ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

174. The method of claim 92, wherein X represents Cl; the ligand comprised by the
5 catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and
trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-
dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-
diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate,
phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or
10 guanidine.

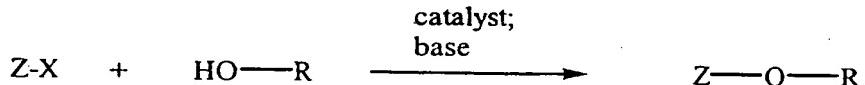
175. The method of claim 92, wherein X represents Cl; the ligand comprised by the
catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-
aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base
is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or
15 sodium hydroxide.

176. The method of claim 92, wherein X represents Cl; the ligand comprised by the
catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane;
and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-
butoxide, or sodium hydroxide.

20 177. The method of claim 92, wherein X represents Cl; the ligand comprised by the
catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-
isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-
(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-
(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline,
25 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-
phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-
(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and
the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-
butoxide, or sodium hydroxide.

30 178. The method of claim 92, wherein X represents Cl; the ligand comprised by the
catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate,
cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

179. The method of claim 92, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 5 180. The method of claim 92, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 10 181. The method of claim 92, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 15 182. A method represented by Scheme 3:



Scheme 3

wherein

- X represents I, Br, Cl, alkylsulfonate, or arylsulfonate;
- 25 Z represents optionally substituted aryl, heteroaryl or alkenyl;
- catalyst comprises a copper atom or ion, and a ligand;
- base represents a Bronsted base; and

R represents optionally substituted alkyl, cycloalkyl, aralkyl, heteroaralkyl, alkenylalkyl, or alkynylalkyl.

183. The method of claim 182, wherein X represents I.
184. The method of claim 182, wherein X represents Br.
- 5 185. The method of claim 182, wherein X represents Cl.
186. The method of claim 182, wherein the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.
187. The method of claim 182, wherein the ligand comprised by the catalyst is an 10 optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.
188. The method of claim 182, wherein the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.
- 15 189. The method of claim 182, wherein the ligand comprised by the catalyst is a chelating 20 ligand.
190. The method of claim 182, wherein the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.
191. The method of claim 182, wherein the ligand comprised by the catalyst is cis-1,2- 25 diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.
- 30 192. The method of claim 182, wherein the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-

diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

193. The method of claim 182, wherein the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 5 194. The method of claim 182, wherein the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
195. The method of claim 182, wherein the catalyst is present in less than or equal to about 10 mol% relative to Z-X.
- 10 196. The method of claim 182, wherein the catalyst is present in less than or equal to about 5 mol% relative to Z-X.
197. The method of claim 182, wherein the catalyst is present in less than or equal to about 1 mol% relative to Z-X.
- 15 198. The method of claim 182, wherein the catalyst is present in less than or equal to about 0.1 mol% relative to Z-X.
199. The method of claim 182, wherein the method is conducted at a temperature less than about 150 C.
200. The method of claim 182, wherein the method is conducted at a temperature less than about 140 C.
- 20 201. The method of claim 182, wherein the method is conducted at a temperature less than about 110 C.
202. The method of claim 182, wherein the method is conducted at a temperature less than about 100 C.
203. The method of claim 182, wherein the method is conducted at a temperature less than about 90 C.
- 25 204. The method of claim 182, wherein the method is conducted at a temperature less than about 50 C.
205. The method of claim 182, wherein the method is conducted at a temperature less than about 40 C.
- 30 206. The method of claim 182, wherein the method is conducted at ambient temperature.
207. The method of claim 182, wherein Z represents optionally substituted aryl.
208. The method of claim 182, wherein Z represents optionally substituted phenyl.

209. The method of claim 182, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.
210. The method of claim 182, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.
211. The method of claim 182, wherein X represents I; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)dacetic acid.
212. The method of claim 182, wherein X represents I; and the ligand comprised by the catalyst is a chelating ligand.
213. The method of claim 182, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.
214. The method of claim 182, wherein X represents I; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.
215. The method of claim 182, wherein X represents I; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.
216. The method of claim 182, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-

aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

217. The method of claim 182, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

218. The method of claim 182, wherein X represents I; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

219. The method of claim 182, wherein X represents I; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

220. The method of claim 182, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

221. The method of claim 182, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a

carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

222. The method of claim 182, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 10 223. The method of claim 182, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 15 224. The method of claim 182, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 20 225. The method of claim 182, wherein X represents I; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 25 226. The method of claim 182, wherein X represents I; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

227. The method of claim 182, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 5 228. The method of claim 182, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 10 229. The method of claim 182, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 15 230. The method of claim 182, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.
- 20 231. The method of claim 182, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.
232. The method of claim 182, wherein X represents Br; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-

phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

233. The method of claim 182, wherein X represents Br; and the ligand comprised by the catalyst is a chelating ligand.

5 234. The method of claim 182, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

235. The method of claim 182, wherein X represents Br; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and 10 trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

15 236. The method of claim 182, wherein X represents Br; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

20 237. The method of claim 182, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

25 238. The method of claim 182, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

30 239. The method of claim 182, wherein X represents Br; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-

- (dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and
5 the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
240. The method of claim 182, wherein X represents Br; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 10 241. The method of claim 182, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 15 242. The method of claim 182, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane,
20 ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
243. The method of claim 182, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
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- 30 244. The method of claim 182, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base

is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

245. The method of claim 182, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; 5 and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
246. The method of claim 182, wherein X represents Br; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-
10 (dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and
15 the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
247. The method of claim 182, wherein X represents Br; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
248. The method of claim 182, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
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249. The method of claim 182, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane,
25 30 ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

250. The method of claim 182, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 5 251. The method of claim 182, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.
- 10 252. The method of claim 182, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.
253. The method of claim 182, wherein X represents Cl; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.
- 20 254. The method of claim 182, wherein X represents Cl; and the ligand comprised by the catalyst is a chelating ligand.
255. The method of claim 182, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.
256. The method of claim 182, wherein X represents Cl; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

257. The method of claim 182, wherein X represents Cl; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.
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258. The method of claim 182, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, 10 fluoride, or guanidine.
259. The method of claim 182, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 15 260. The method of claim 182, wherein X represents Cl; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline,
- 20 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 25 261. The method of claim 182, wherein X represents Cl; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
262. The method of claim 182, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
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263. The method of claim 182, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 10 264. The method of claim 182, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 15 265. The method of claim 182, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 20 266. The method of claim 182, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 25 267. The method of claim 182, wherein X represents Cl; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-

(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

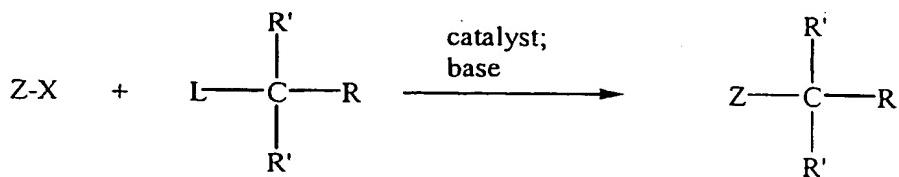
268. The method of claim 182, wherein X represents Cl; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

269. The method of claim 182, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

10 270. The method of claim 182, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

20 271. The method of claim 182, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

25 272. A method represented by Scheme 4:



Scheme 4

wherein

- X represents I, Br, Cl, alkylsulfonate, or arylsulfonate;
- Z represents optionally substituted aryl, heteroaryl or alkenyl;
- L represents H or a negative charge;
- 5 catalyst comprises a copper atom or ion, and a ligand;
- base represents a Bronsted base;
- R represents H, optionally substituted alkyl, cycloalkyl, aralkyl, aryl, or heteroaryl;
- R' represents independently for each occurrence H, alkyl, cycloalkyl, aralkyl, aryl, or heteroaryl, formyl, acyl, -CO₂R'', -C(O)N(R)₂, sulfonyl, -P(O)(OR'')₂, -CN, or -NO₂;
- 10 R'' represents independently for each occurrence optionally substituted alkyl, cycloalkyl, aralkyl, aryl, or heteroaryl; and
- C(R')₂(R) taken together may represent nitrile.
273. The method of claim 272, wherein X represents I.
274. The method of claim 272, wherein X represents Br.
- 15 275. The method of claim 272, wherein X represents Cl.
276. The method of claim 272, wherein the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.
277. The method of claim 272, wherein the ligand comprised by the catalyst is an 20 optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.
278. The method of claim 272, wherein the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'- 25 tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.
279. The method of claim 272, wherein the ligand comprised by the catalyst is a chelating 30 ligand.

280. The method of claim 272, wherein the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.
281. The method of claim 272, wherein the ligand comprised by the catalyst is cis-1,2-
5 diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2- diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2- diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-
10 dimethyl-1,2-diaminoethane.
282. The method of claim 272, wherein the ligand comprised by the catalyst is cis-1,2- diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2- diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2- diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or
15 N,N'-dimethyl-1,2-diaminoethane.
283. The method of claim 272, wherein the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
284. The method of claim 272, wherein the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 20 285. The method of claim 272, wherein the catalyst is present in less than or equal to about 10 mol% relative to Z-X.
286. The method of claim 272, wherein the catalyst is present in less than or equal to about 5 mol% relative to Z-X.
- 25 287. The method of claim 272, wherein the catalyst is present in less than or equal to about 1 mol% relative to Z-X.
288. The method of claim 272, wherein the catalyst is present in less than or equal to about 0.1 mol% relative to Z-X.
289. The method of claim 272, wherein the method is conducted at a temperature less than about 150 C.
- 30 290. The method of claim 272, wherein the method is conducted at a temperature less than about 140 C.

291. The method of claim 272, wherein the method is conducted at a temperature less than about 110 C.
292. The method of claim 272, wherein the method is conducted at a temperature less than about 100 C.
- 5 293. The method of claim 272, wherein the method is conducted at a temperature less than about 90 C.
294. The method of claim 272, wherein the method is conducted at a temperature less than about 50 C.
295. The method of claim 272, wherein the method is conducted at a temperature less
10 than about 40 C.
296. The method of claim 272, wherein the method is conducted at ambient temperature.
297. The method of claim 272, wherein Z represents optionally substituted aryl.
298. The method of claim 272, wherein Z represents optionally substituted phenyl.
299. The method of claim 272, wherein R represents H.
- 15 300. The method of claim 272, wherein R' represents independently for each occurrence acyl, or -CO₂R".
301. The method of claim 272, wherein R" represents independently for each occurrence alkyl, cycloalkyl, or aralkyl.
302. The method of claim 272, wherein X represents I; and the ligand comprised by the
20 catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.
303. The method of claim 272, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.
304. The method of claim 272, wherein X represents I; and the ligand comprised by the
25 catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-
30 phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.

305. The method of claim 272, wherein X represents I; and the ligand comprised by the catalyst is a chelating ligand.
306. The method of claim 272, wherein X represents I; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.
- 5 307. The method of claim 272, wherein X represents I; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-
- 10 diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.
308. The method of claim 272, wherein X represents I; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and
- 15 trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.
309. The method of claim 272, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-
- 20 aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
310. The method of claim 272, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane;
- 25 and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
311. The method of claim 272, wherein X represents I; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-
- 30 (dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-

phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

5 312. The method of claim 272, wherein X represents I; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

313. The method of claim 272, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

10 314. The method of claim 272, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-15 dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, 20 or guanidine.

315. The method of claim 272, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-25 dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

316. The method of claim 272, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

317. The method of claim 272, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 5 318. The method of claim 272, wherein X represents I; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline,
- 10 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 15 319. The method of claim 272, wherein X represents I; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
320. The method of claim 272, wherein X represents I; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 20 321. The method of claim 272, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
- 25 322. The method of claim 272, wherein X represents I; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and
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trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

323. The method of claim 272, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

324. The method of claim 272, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

325. The method of claim 272, wherein X represents Br; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-

15 (dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)dacetic acid.

326. The method of claim 272, wherein X represents Br; and the ligand comprised by the catalyst is a chelating ligand.

327. The method of claim 272, wherein X represents Br; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.

328. The method of claim 272, wherein X represents Br; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.

329. The method of claim 272, wherein X represents Br; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and

trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.

330. The method of claim 272, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

331. The method of claim 272, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

332. The method of claim 272, wherein X represents Br; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

333. The method of claim 272, wherein X represents Br; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

334. The method of claim 272, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

335. The method of claim 272, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-

- dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
336. The method of claim 272, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
337. The method of claim 272, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
338. The method of claim 272, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.
339. The method of claim 272, wherein X represents Br; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

340. The method of claim 272, wherein X represents Br; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

341. The method of claim 272, wherein X represents Br; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

342. The method of claim 272, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

343. The method of claim 272, wherein X represents Br; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

344. The method of claim 272, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline.

345. The method of claim 272, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane.

346. The method of claim 272, wherein X represents Cl; and the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-

- (dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid.
- 5 347. The method of claim 272, wherein X represents Cl; and the ligand comprised by the catalyst is a chelating ligand.
348. The method of claim 272, wherein X represents Cl; and the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane.
- 10 349. The method of claim 272, wherein X represents Cl; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane.
- 15 350. The method of claim 272, wherein X represents Cl; and the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane.
- 20 351. The method of claim 272, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 25 352. The method of claim 272, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.
- 30 353. The method of claim 272, wherein X represents Cl; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-

isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

354. The method of claim 272, wherein X represents Cl; the ligand comprised by the catalyst is a chelating ligand; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

355. The method of claim 272, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

356. . The method of claim 272, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane, ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

357. The method of claim 272, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is a carbonate, phosphate, oxide, hydroxide, alkoxide, aryloxide, amine, metal amide, fluoride, or guanidine.

358. The method of claim 272, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted aryl alcohol, alkyl amine, 1,2-diamine, 1,2-aminoalcohol, 1,2-diol, imidazolium carbene, pyridine, or 1,10-phenanthroline; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or 5 sodium hydroxide.

359. The method of claim 272, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted phenol, 1,2-diaminocyclohexane, or 1,2-diaminoalkane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

10 360. The method of claim 272, wherein X represents Cl; the ligand comprised by the catalyst is selected from the group consisting of 2-phenylphenol, 2,6-dimethylphenol, 2-isopropylphenol, 1-naphthol, 8-hydroxyquinoline, 8-aminoquinoline, DBU, 2-(dimethylamino)ethanol, ethylene glycol, N,N-diethylsalicylamide, 2-(dimethylamino)glycine, N,N,N',N'-tetramethyl-1,2-diaminoethane, 1,10-phenanthroline, 15 4,7-diphenyl-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 5-methyl-1,10-phenanthroline, 5-chloro-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4-(dimethylamino)pyridine, 2-(aminomethyl)pyridine, and (methylimino)diacetic acid; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

20 361. The method of claim 272, wherein X represents Cl; the ligand comprised by the catalyst is a chelating ligand; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

362. The method of claim 272, wherein X represents Cl; the ligand comprised by the catalyst is an optionally substituted 1,2-diaminocyclohexane, 1,10-phenanthroline, 2-hydroxyethyl amine, or 1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

25 363. The method of claim 272, wherein X represents Cl; the ligand comprised by the catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-diaminocyclohexane, cis-N-tolyl-1,2-diaminocyclohexane, trans-N-tolyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N-tolyl-1,2-diaminocyclohexane,

ethanolamine, 1,2-diaminoethane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium hydroxide.

364. The method of claim 272, wherein X represents Cl; the ligand comprised by the
5 catalyst is cis-1,2-diaminocyclohexane, trans-1,2-diaminocyclohexane, a mixture of cis- and
trans-1,2-diaminocyclohexane, cis-N,N'-dimethyl-1,2-diaminocyclohexane, trans-N,N'-
dimethyl-1,2-diaminocyclohexane, a mixture of cis- and trans-N,N'-dimethyl-1,2-
diaminocyclohexane, or N,N'-dimethyl-1,2-diaminoethane; and the base is potassium
phosphate, potassium carbonate, cesium carbonate, sodium *tert*-butoxide, or sodium
10 hydroxide.

Figure 1

Amination of different aryl iodides with benzylamine

Entry	ArI	Products	Time/h	% Yield ^a	
				1 mol% CuI, K ₂ PO ₄ , 2 equiv. ethylene glycol isopropanol, 80 °C	10 mol% CuI, 1 mol% CuI, n-BuLi solvent, 100 °C, 1.0 mmol amine, 1.4 mmol ArI was used. 2 equiv. of benzylamine was used. Etanol was used as solvent.
1	Ph-I	Ph-NH-Ph	18 ^b	91	89
2	O-C(=O)-Ph-I	O-C(=O)-Ph-NH-Ph	5 ^b 15 ^b (70 °C)	90	87
3	N≡C-Ph-I	N≡C-Ph-NH-Ph	12	78	
4	Cl-Ph-I	Cl-Ph-NH-Ph	12	84	
5	MeO-Ph-I	MeO-Ph-NH-Ph	18	69	
6	Me-Ph-I	Me-Ph-NH-Ph	18	86	
7	2- <i>i</i> -Pr-Ph-I	2- <i>i</i> -Pr-Ph-NH-Ph	12 ^c	82	85
8	2-Br-Ph-I	2-Br-Ph-NH-Ph	12 ^c	83	87
9	2-Cl-Ph-I	2-Cl-Ph-NH-Ph	12 ^c	86	86
10	2- <i>t</i> -Bu-Ph-I	2- <i>t</i> -Bu-Ph-NH-Ph	12 ^c	82	85
11	2- <i>m</i> -Br-Ph-I	2- <i>m</i> -Br-Ph-NH-Ph	30 ^c		
12	2- <i>m</i> -Cl-Ph-I	2- <i>m</i> -Cl-Ph-NH-Ph	12 ^c	80	
13	2- <i>m</i> -CN-Ph-I	2- <i>m</i> -CN-Ph-NH-Ph	12 ^c	91	85
14	2- <i>m</i> -FCF ₃ -Ph-I	2- <i>m</i> -FCF ₃ -Ph-NH-Ph	18 ^c		
15	2- <i>m</i> -OMe-Ph-I	2- <i>m</i> -OMe-Ph-NH-Ph	18	60	
16	2- <i>m</i> -NO ₂ -Ph-I	2- <i>m</i> -NO ₂ -Ph-NH-Ph	12 ^c	72	
17	2- <i>m</i> -Me-Ph-I	2- <i>m</i> -Me-Ph-NH-Ph	12 ^c	87	
18	2- <i>m</i> -MeO-Ph-I	2- <i>m</i> -MeO-Ph-NH-Ph	12 ^c	69	
19	2- <i>m</i> -OMe-Ph-I	2- <i>m</i> -OMe-Ph-NH-Ph	72 ^d	73	
20	2- <i>m</i> -Me-Ph-I	2- <i>m</i> -Me-Ph-NH-Ph	72 ^d	73	
21	2- <i>m</i> -OMe-Ph-I	2- <i>m</i> -OMe-Ph-NH-Ph	72 ^d	73	
22	2- <i>m</i> -X-Ph-I	2- <i>m</i> -X-Ph-NH-Ph	18 ^b	71	
23	2- <i>m</i> -X-Ph-I	2- <i>m</i> -X-Ph-NH-Ph	40 ^b	53	
24	2- <i>m</i> -X-Ph-I	2- <i>m</i> -X-Ph-NH-Ph	72 ^b	48	
25	2- <i>m</i> -OH-Ph-I	2- <i>m</i> -OH-Ph-NH-Ph	24	95	
26	H ₂ N-Ph-I	H ₂ N-Ph-NH-Ph	36 ^d (80 °C)	82	
27	EIOOC-Ph-I	EIOOC-Ph-NH-Ph	12 ^b	50	
28	2- <i>m</i> -Naph-I	2- <i>m</i> -Naph-NH-Ph	12	70	

^a Isolated yield was reported in average of 2 run. ^b 1 mol% CuI. ^c 10 mol% CuI. ^d The reaction was conducted under air. ^e n-BuLi solvent, 10 mol% CuI, 100 °C, 1.0 mmol amine, 1.4 mmol ArI was used. ^f 2 equiv. of benzylamine was used. ^g Ethanol was used as solvent.

Figure 2

Amination of iodobenzene with different amines

Entry	Amines	Products	Time/h	% Yield*
1	H ₂ N—Ph		8	91
2	H ₂ N—(CH ₂) ₅		12 ^b	84
3			30 ^b	80
4			18 ^d	82
5	H ₂ N—CH ₂ OMe		18 ^b	91
6			30 ^b	87
7			18 ^d	85
8			24	73
9			24	76 (99%ee)
10			24	70 (74%)
11			18 ^b	90
12			30 ^b	89
13			18 ^d	84
14			18	80
15			10	76
16			10	71
17			24	70
18			36 ^c (90°C)	41
19			12 (90 °C)	O-arylated ethylene glycol was observed.
20			12 (90 °C)	O-arylated ethylene glycol was observed.
21			36 (90°C)	50

* Isolated yield was reported in average of 2 run. ^b 1 mol% CuI. ^c 10 mol% CuI. ^d The reaction was conducted under air. ^e 10% CuI, ^f BuOH solvent at 90 °C.

Figure 3

Amination of aryl iodides with amines					
	ArI	Amines	Products	Time/h	%Yield ^a
					(3)
	1.0 mmol	1.2 mmol			
				5 mol% CuI, K3PO4 2 equiv. ethylene glycol isopropanol, 80 °C	
1				14 ^b	70
2				14 ^b	85
3				22	87
4				22	69
5				24	88
6				23 ^c	73

^a Isolated yield was reported. ^b n-Butanol solvent was used, 100 °C.
^c 1.2 mmol of ArI and 0.5 mmol of amine was used.

Figure 4**Table 4. Amination of Bromobenzene in the Presence of Substituted Phenols.**

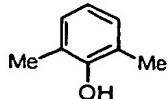
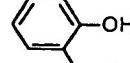
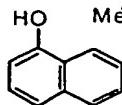
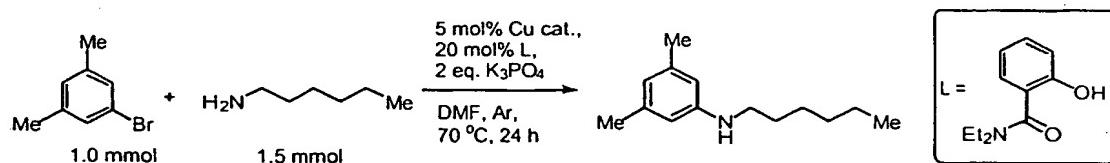
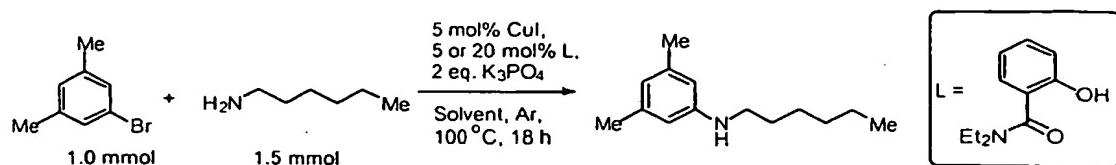
Entry	ArOH	% Conv.	GC yield%
1		57	56% GC yield.
2		99	45% GC yield
3		75	61% GC yield

Figure 5

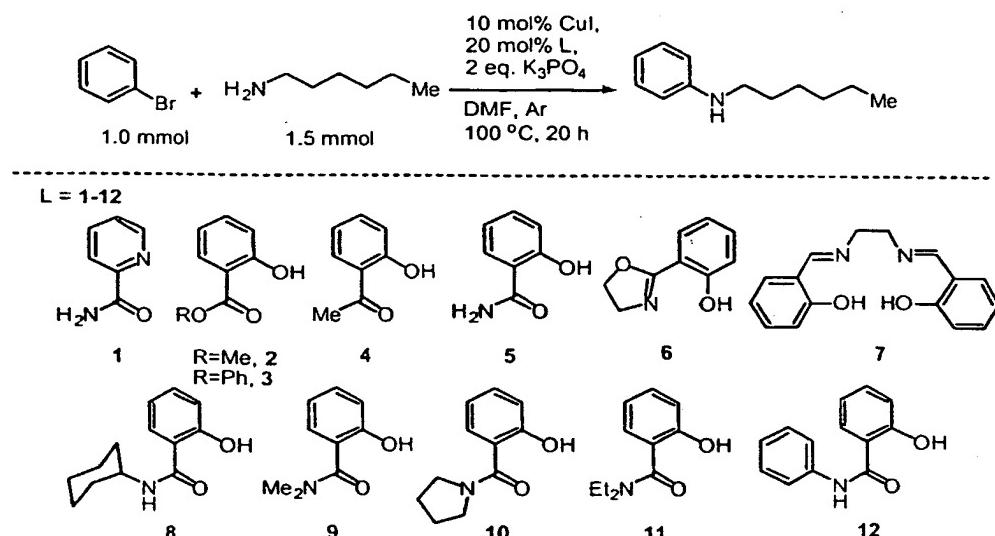
Entry	Cu Complex	% Conv. ^a	% Yield ^b
1	CuI	68	67
2	CuCl	83 (100) ^c	83 (>99) ^c
3	CuBr	82 (99) ^c	82 (99) ^c
4	CuOAc	89 (>99) ^c	89 (99) ^c
5	CuCl ₂ •H ₂ O	49	42
6	CuBr ₂	53	47
7	CuF ₂	24	6
8	Cu(OAc) ₂	57 (99) ^c	53 (98) ^c
9	Cu(acac) ₂	60	56
10	Cu(OTf) ₂	55	50
11	CuSO ₄ •5H ₂ O	44	35

^aCalibrated GC conversion. ^bCalibrated GC yield. ^cYields in parentheses were obtained for reactions performed at 90 °C for 20 h.

Figure 6

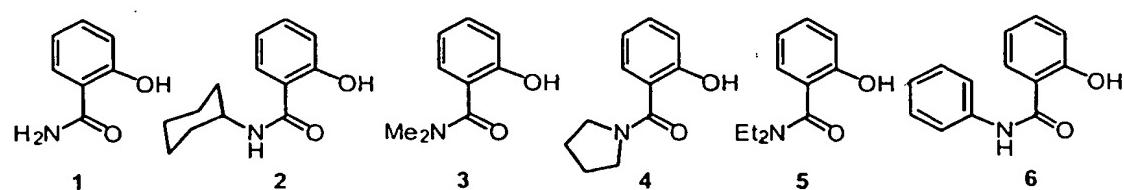
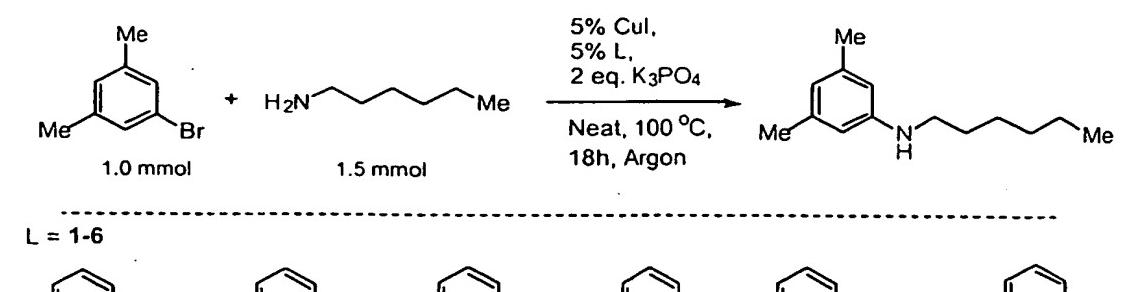
		CuI:L = 1:1		CuI:L = 1:4	
Entry	Solvent	%Conv. ^a	% Yield ^b	%Conv. ^a	% Yield ^b
1	Neat	91	88	88	80
2	DMF	70	66	94	90
3	NMP	13	Trace	77	69
4	Et ₃ N	9	Trace	39	33
5	iPr ₂ NH	10	4	25	28
6	Toluene	56	50	59	53
7	DME	68	63	76	69
8	Dioxane	65	60	83	79
9	DMF:Tol = 1:1	/	/	95	92
10	DMF:Tol = 1:4	/	/	89	83
11	DMF:Tol = 1:9	/	/	78	73

^aCalibrated GC conversion. ^bCalibrated GC yield.

Figure 7

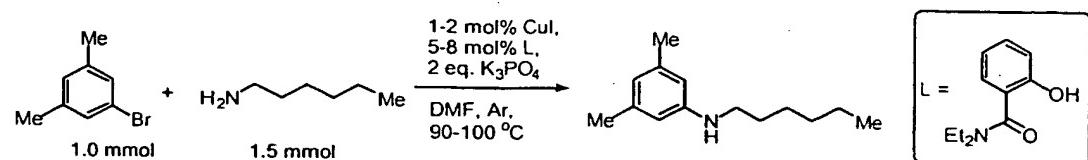
Entry	Ligand	% Conv. ^a	% yield ^b
1	1	90	27
2	2	94	64
3	3	95	79
4	4	46	38
5	5	70	64
6 ^c	6	55	47
7 ^c	7	60	35
8 ^c	8	41	36
9 ^c	9	99	99
10 ^c	10	99	99
11 ^c	11	99	99
12 ^c	12	67	64

Figure 8



Entry	Ligand	% Conv. ^a	% yield ^b
1	1	71	66
2	2	11	8
3	3	93	90
4	4	83	79
5	5	93	92
6	6	65	65

^aCalibrated GC conversion. ^bCalibrated GC yield.

Figure 9

Entry	CuI and L	Temp./ °C	Time/ h	% Conv. ^a	% Yield ^b
1	2% CuI, 8% L	100	24	87	86
2	2% CuI, 8% L	100	42	98	96 (90 iso.)
3	1% CuI, 5% L	90	54	85	83
4 (control)	5% CuI, 20% L	100	18	97	95

^aCalibrated GC conversion. ^bCalibrated GC yield.

Figure 10

1.0 mmol 1.5 mmol 5 mol% CuI, 20 mol% L,
 2 eq. K_3PO_4 ,
 DMF, Ar,
 90 °C, 18-22 h Product

L =

 $Et_2N-C(=O)-CH_2-Ph-OH$

Entry	ArBr	Amine	Product	%Conv.	% yield ^a
1		$H_2N-CH_2-CH_2-CH_2-CH_2-CH_3$		98	91
2		$H_2N-CH_2-CH_2-CH_2-CH_2-CH_3$		96	80
3		$H_2N-CH_2-CH_2-CH_2-OH$		99	90
4		$Cyclohexyl-CH_2-CH_2-NH_2$		>99	95
5		$H_2N-CH_2-C_6H_4-CH_3$		99	88
6		$H_2N-CH_2-C_6H_4-CH_3$		99	84
7		$H_2N-CH_2-C_6H_4-O$		96	87
8		$H_2N-CH_2-CH_2-CH_2-CH_2-CH_3$		>99	72
9		H_2N-CH_2-OMe		>99	77
10		$H_2N-CH_2-CH_2-CH_2-CH_3$		99	78
11		$H_2N-CH_2-Cyclohexyl-NH$		>99	62

^a Isolated yield was reported.

Figure 11

$\text{ArBr} \quad 1.0 \text{ mmol}$ $\text{H}_2\text{NR} \quad 1.5 \text{ mmol}$ $\xrightarrow[\text{90 } ^\circ\text{C, 18-22 h}]{\substack{\text{5 mol% CuI,} \\ \text{20 mol% L,} \\ \text{2 eq. K}_3\text{PO}_4, \\ \text{DMF, Ar}}}$ Product

$L =$

Entry	ArBr	Amine	Product	%Conv.	% yield ^a
1		$\text{H}_2\text{N}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_3$		95	89 @ 100°C
2		$\text{H}_2\text{N}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_3$		>99	81
3		$\text{H}_2\text{N}-\text{CH}_2-\text{Cyclohexyl}$		96	79 @ 100°C
4 ^b		$\text{H}_2\text{N}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_3$		>99	83
5 ^c		$\text{H}_2\text{N}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_3$		>99	81 @ 100°C
6				>99	83
7		$\text{H}_2\text{N}-\text{CH}_2-\text{Cyclohexyl}$		99	82
8		$\text{H}_2\text{N}-\text{CH}_2-\text{C}_6\text{H}_4-\text{OMe}$		95	85

^a Isolated yield. ^b 1.2 mmol of amine was used. ^c 4.0 mmol of amine was used, 42 hours.

Figure 12

$\text{ArBr} \quad 1.0 \text{ mmol}$ $\text{H}_2\text{NR} \quad 1.5 \text{ mmol}$ $\xrightarrow[100^\circ\text{C}, 18-22\text{h}]{\substack{5 \text{ mol\% CuI,} \\ 5 \text{ mol\% L,} \\ 2 \text{ eq. K}_3\text{PO}_4}}$ Product

$L =$

Entry	ArBr	Amine	Product	%Conv.	%yield ^a
1				95	90
2				22	9 ^b
				11	0 (NaO'iBu)
3				90	89 ^c
4				96	59
5				98	71
6				99	92
7				>99	60
8				>99 @ 90°C	82

^a Isolated yield was reported. ^b GC yield was reported. ^c average of 2 run.

Figure 13

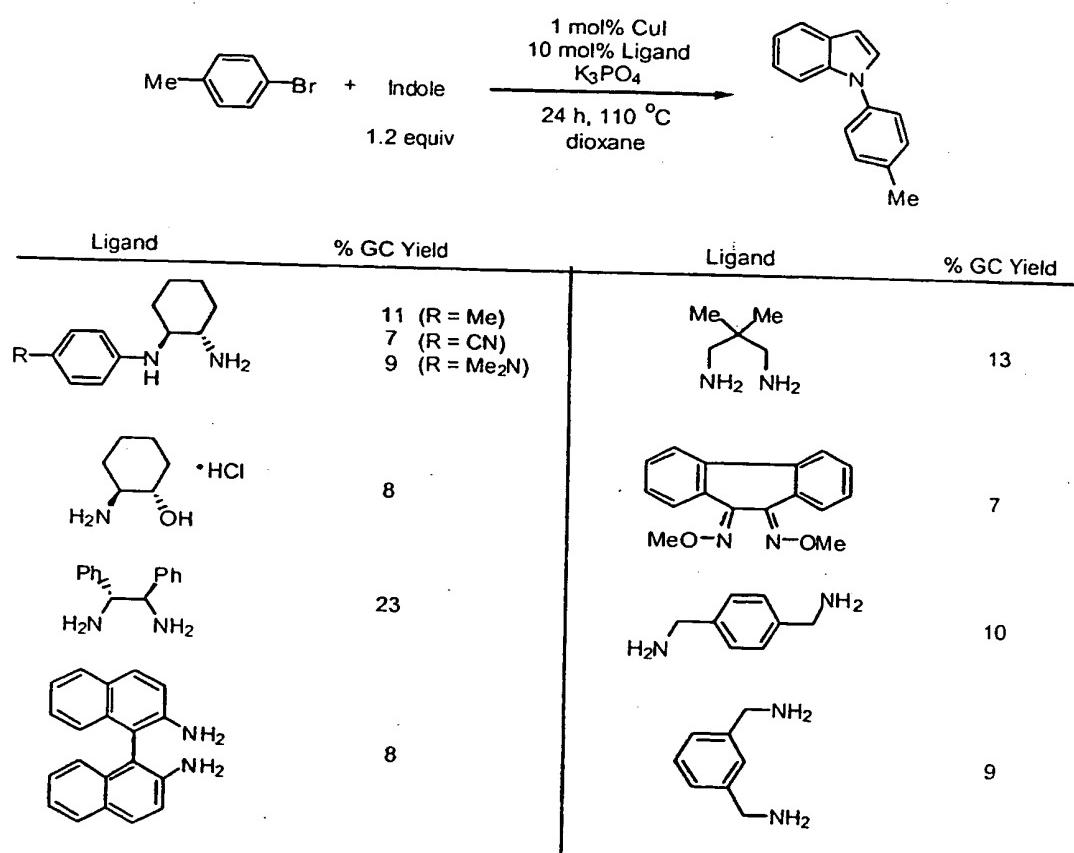
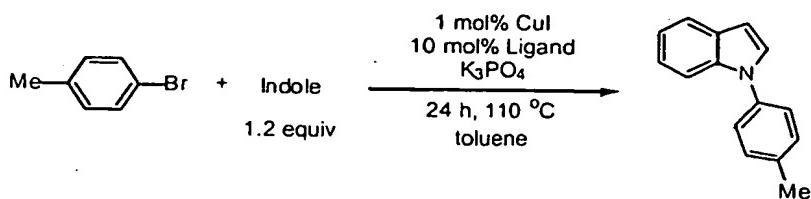
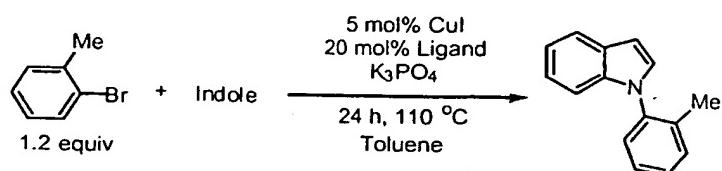


Figure 14

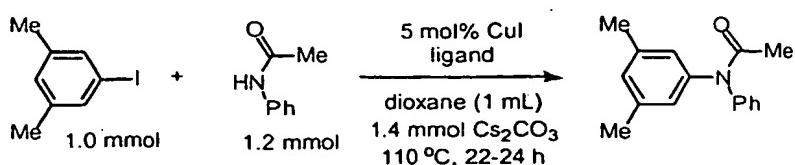
Ligand	% GC Yield	Ligand	% GC Yield
	98		12
	9		37
	5		50
	5		71
	6		60
			11

Figure 15



Ligand	% GC Yield	Ligand	% GC Yield
	58 (4h)		25
	6		1
	1		4
	8		3
	7		4
	3		42

Figure 17

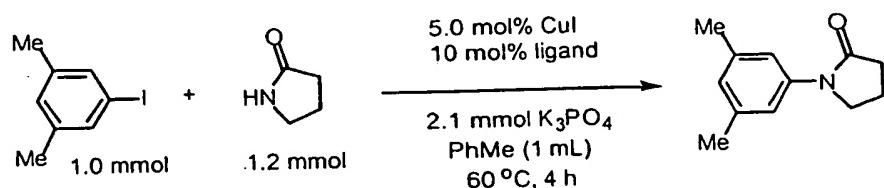


Entry	Ligand	Amount of ligand (mol%)	GC yield
1		22	76% ^a
2		11	22%
3		12	36%
4		10	77%
5		10	47%
6		10	52% ^b

^a 1.7 mmol of Cs₂CO₃ was used. ^b 2.1 mmol K₃PO₄ was used instead of Cs₂CO₃.

Figure 16

Ligand	% GC Yield	Ligand	% GC Yield
	9		1
	2		40
	26		3
	51		2
	8		3
	8		5

Figure 18

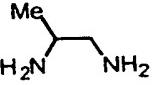
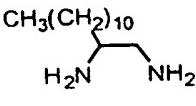
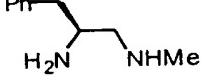
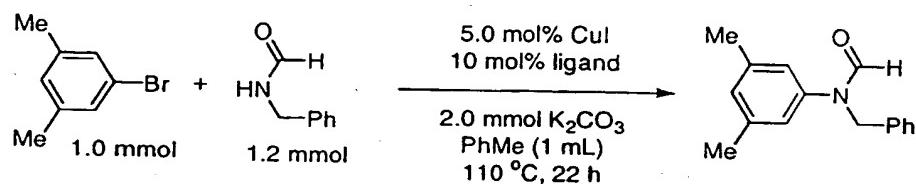
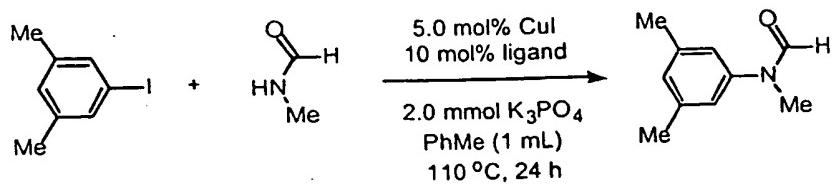
Entry	Ligand	GC yield (%)
1		50%
2		51%
3		95%

Figure 19

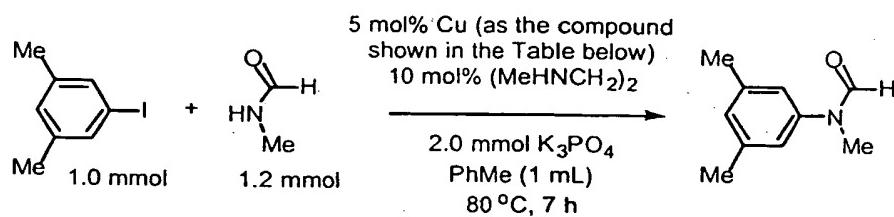


Entry	Ligand	GC yield	Entry	Ligand	GC yield
1		26%	7 ^b		52%
2		84%	8 ^c		39%
3		92%	9 ^d		93%
4		84%	10 ^e		39%
5		12%			
6 ^a		33%			

^a Racemic *trans*-isomer of the ligand. ^b *cis*-Isomer of the ligand. ^c The commercial mixture of the *cis*- and *trans*-isomers of the ligand. ^d Racemic *trans*-isomer of the ligand. ^e Racemic *trans*-isomer of the ligand.

Figure 20

Entry	Ligand	GC yield
1	Ph ₃ P	39%
2	(MeO) ₃ P	55%
3	Ph ₃ As	37%
4		75%
5		74%
6		56%

Figure 21

Entry	Copper Compound	GC yield
1	Cu powder	86%
2	CuI	97%
3	CuCl	93%
4	CuSCN	85%
5	Cu_2O	91%
6	CuCl_2	55%
7	$\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$	79%
8	Cu(II) acetate	71%
9	Cu(II) acetylacetone	83%

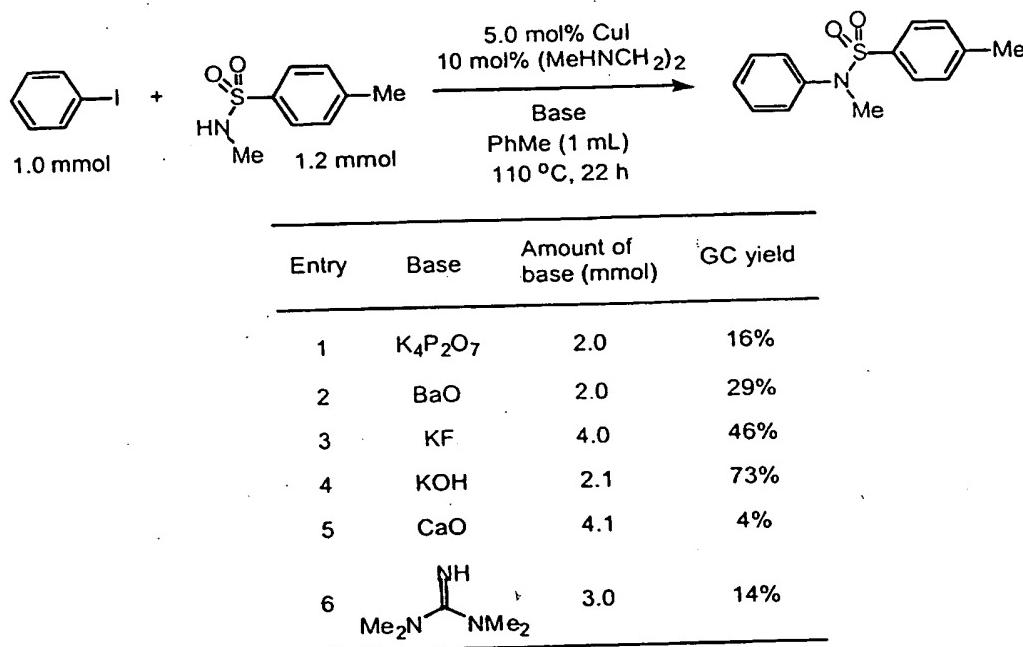
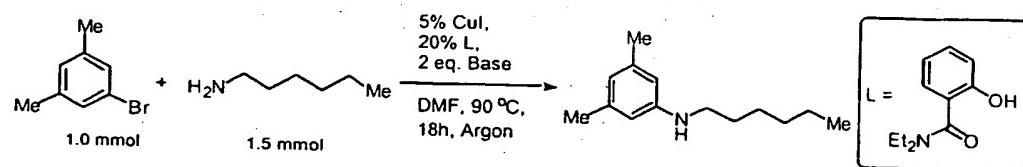
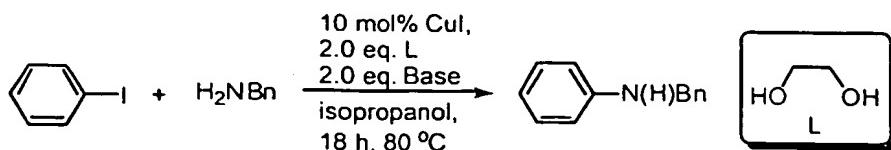
Figure 22

Figure 23



Entry	Base	%Conv. ^a	%Yield ^b
1	K_3PO_4	98	96
2	$\text{K}_3\text{PO}_4 \cdot \text{H}_2\text{O}$	36	28
3	Na_3PO_4	28	8
4	Li_3PO_4	30	2
5	Cs_2CO_3	85	83
6	K_2CO_3	74	71
7	Na_2CO_3	31	4
8	Li_2CO_3	30	2
9	NaOH	17	1
10	KOH	20	1
11	$\text{K}_4\text{P}_2\text{O}_7$	31	3
12	KOAc	41	14
13	DBU	25	1

^aConversion of 5-bromo-*m*-xylene based on GC integration. ^bCalibrated GC yield.

Figure 24

Entry	Base	%Conv. ^a	%Yield ^b
1	K ₃ PO ₄	98	93
2	K ₂ CO ₃	34	10
3	Cs ₂ CO ₃	99	77
4	NaO ^t Bu	77	43
5	NaOH	72	26
6	KOH	58	29

^aConversion of iodobenzene based on GC integration. ^bCalibrated GC yield.

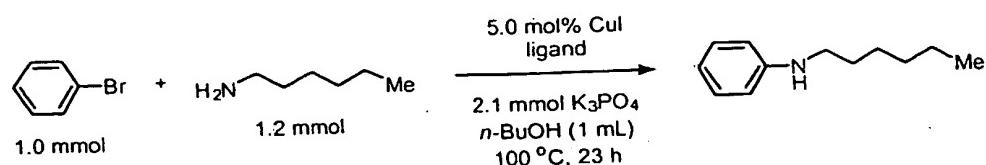
Figure 25

Ic1ccccc1 + H2N-Bn $\xrightarrow[18\text{ h}, 80^\circ\text{C}]{10\text{ mol\% CuI, diol, 2.0 eq. K}_3\text{PO}_4 \text{ in isopropanol}}$ c1ccccc1-N(H)Bn

entry	diol	equiv of diol	conv, %	yield, % ^b
1		0.1	27	5
2		0.2	34	10
3		0.5	52	42
4		1.0	80	77
5		2.0	98	93 (87 ^c)
6		2.0	20	trace
7		2.0	21	trace
8		2.0	53	34
9		2.0	29	trace (42 ^c)
10		2.0	44	31
11		2.0	49	33
12		2.0	52	27
13		2.0	20	7 (38 ^c)
14		2.0	32	17 (31 ^c)
15		2.0	29	18 (14 ^c)
16	sucrose	2.0	5	trace

^a Reaction conditions: 1.0 mmol iodobenzene, 1.2 mmol benzylamine, 10 mol% CuI, 2.0 mmol diol, 2.0 mmol K₃PO₄, iPrOH (1 mL), 80 °C under Ar. ^b Calibrated GC yield. ^c Diol used as solvent.

Figure 26



Entry	Ligand	Amount of ligand (mmol)	GC yield
1		2.0	63%
2		0.50	48%
3		0.50	7%
4		0.50	11%
5		0.50	16%

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/12785

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07C 209/06, 209/08, 209/10, 209/22
 US CL : 564/395, 404, 405, 469, 481

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 U.S. : 564/395, 404, 405, 469, 481

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4,764,625 A (TURNER et al.) 16 August 1988 (16.08.1988), whole document.	1-364

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Date of the actual completion of the international search

11 July 2002 (11.07.2002)

Date of mailing of the international search report

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